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NEW WORK **JUST READY**

A TREATISE ON

TUMORS

FOR THE USE OF PHYSICIANS AND SURGEONS

By ARTHUR E. HERTZLER, M.D.

of Kansas City, Mo., Assistant Professor of Surgery in the University of Kansas.

Octavo, 728 pages, with 538 illustrations and 8 plates. Cloth, $7.00, net; half Persian morocco, gilt top, de luxe, $9.00, net.

The enormous importance of tumors arises from many factors. Tracing their origin to many pathological causes, and capable of invading every tissue in the body, they are among the most frequent of human afflictions. Even if they were in themselves always benign, the obstruction they cause in normal functions and the deformity they frequently present would often call for surgical intervention. When to all this is added the fact that tumors are the most frequent starting point of cancer, with its prolonged agonies, and that early recognition and extirpation are the only cure, the necessity of a special volume, bringing the general practitioner and the surgeon into co-operation, is manifest. Such a work Professor Hertzler has undertaken to provide. It is the result of many years of research and practice. The author has presented his full and mature knowledge, embodying familiarity with the literature of the subject, the observations of laboratory study and long experience in operating and its results. His work, profusely illustrated with original drawings, is one of prime importance to students, practitioners, surgeons and specialists.

FROM THE PREFACE

This treatise embodies the experience of many years gained in the operating-room, the observations of laboratory study and the information gathered in the library, combined in such proportions as my duties in teaching students and as a surgical consultant have shown to be most advisable.

The aim of the book is to give students and practitioners a guide to the proper recognition of tumors. Available books dealing with this subject are either broadly clinical or entirely scientific. A proper comprehension of any tumor demands the application of both the scientific viewpoint and clinical observation. The aim has been to supply this need. For this purpose it was thought best to place the chief emphasis upon the practical aspects of the subject and to include as well sufficient of the more abstract considerations to make the practical side broadly intelligible.

In view of the essentially practical character of the work, the vast field of experimental oncology has been entirely omitted because, in the first place, the results, promising as they are, have not yet attained a state of practical utility, and would but confuse the student and practitioner; and, in the second place, those who are engaged in tumor research necessarily work in laboratories where experienced personal guidance is available.

Citations of literature have been incorporated particularly in those chapters where existent opinion is still divergent. These are presented that the student may follow the subject and as an apology for the unqualified presentation of the author's viewpoints. Papers with bibliographies most likely to be accessible to the reader have received preference.

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THE

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MARCH, 1912

ORIGINAL ARTICLES

THE FUNCTIONAL DIAGNOSIS OF PANCREATIC DISEASE.[1]

By Joseph H. Pratt, M.D.,

of Boston, Mass.

(From the Laboratory of the Theory and Practice of Physic, Harvard University, and the Massachusetts General Hospital.)

In the preface of his classical work on diseases of the pancreas, Oser[2] says that there is perhaps with no organ in the human body such a disparity between the height of its physiological importance and the low level of our clinical knowledge as with the pancreas. This statement is true today despite the advances that have been made during the fourteen years that have elapsed since Oser published his monograph.

It strikes one as strange that so little should be known about the diseases of an organ which plays such an important part in digestion and in intermediate metabolism as does the pancreas. It is the only gland which furnishes an enzyme for each of the three chief classes of organic foodstuffs. The activated proteolytic ferment, trypsin, breaks down the native proteins into simpler bodies than does the pepsin of the gastric juice. Steapsin splits the neutral fat of the food into glycerine and fatty acids. The third ferment, diastase, converts starch into sugar. The volume of pancreatic juice secreted in a day may amount to half a liter or more (Glaessner).

The importance of the pancreas in the metabolism of sugar is undoubted, although the way in which the pancreas acts is unknown.

[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, January 22, 1912. The investigations which furnished the material for this paper were made with the aid of grants from the Proctor Fund for the Study of Chronic Diseases.

[2] Die Erkrankungen des Pancreas, Nothnagel's Spec. Path. u. Ther., Vienna, 1898, I

Amid much that is obscure one fact is clear. The total removal of the gland is always followed by diabetes which runs a rapidly fatal course.

It was formerly held that if the pancreatic juice was entirely excluded from the intestine a serious disturbance took place in the digestion of nitrogenous food, fats, and starches. This seems clearly proved by the experiments of Minkowski and Abelmann, who found, after total extirpation of the pancreas in dogs, that very little of the fat and nitrogen was absorbed. In a few cases of extensive disease of the pancreas clinical observers had noted that the stools were fatty and contained many muscle fibers. Hence the conclusion that in pancreatic disease there was poor absorption of fat and nitrogen.

New studies beginning with those of Friedrich Müller[3] threw doubt on the correctness of the accepted views. Müller showed clearly by careful chemical studies that steatorrhea was not pathognomonic of pancreatic disease, for fatty stools occurred in icterus. He claimed, moreover, that in pancreatic disease unassociated with jaundice there was no disturbance in the assimilation of fat and nitrogen.

Within the last few years several researches on the effect of tying the pancreatic ducts have been published in Europe. The results of these animal experiments supported the clinical observations of Müller. (Lombroso,[4] Zunz and Mayer,[5] Niemann,[6] and and Fleckseder.[7]) Quantitative analyses of the feces seemed to show that little or no disturbance in the utilization of the fat and nitrogen of the food resulted from shutting out the pancreatic juice from the intestine. The statement made by Brugsch[8] in a recent paper is in accord with the present views of A. Schmidt, Minkowski, and other German authorities. Brugsch said that the absence of pancreatic tissue and not the exclusion of the pancreatic juice from the intestine leads to disturbances in absorption. How a portion of the pancreas separated from the intestine by complete occlusion of the ducts can influence the digestion and absorption of food is not explained.

Observations made in our laboratory have shown the error of these views. We found that total exclusion of the pancreatic juice from the intestine always resulted in a great decrease in the assimilation of fats and proteins. As soon as the animal recovered from the operation and began to take food in quantity the stools became very large, soft, and fatty. There were usually several movements a day. On microscopic examination the feces were found to consist largely of undigested muscle fibers. In spite of ravenous appetites

[3] Zeitsch. f. klin. Med., 1887, xii, 45.
[4] Arch. f. exp. Path. u. Pharm., 1908, lix, 251.
[5] Mém. couronnées et autres mém. p. p. l'Acad. Royale de Méd. de Belgique, 1906, xviii, 7. Quoted by Hess.
[6] Zeitsch. f. exp. Path. u. Ther., 1909, v, 466.
[7] Arch. f. exp. Path. u. Pharm., 1909, lix, 407.
[8] Deutsch. med. Woch., 1909, xxxv, 2307.

the dogs lost weight rapidly. Since the publication of the paper of Pratt, Lamson, and Marks,[9] additional experiments made by Dr. Murphy and me have yielded confirmatory results. It is a difficult matter to exclude all the pancreatic juice from the intestine, and failure to do so explains the results obtained by other investigators. In a search of the literature I found that Hess[10] had clearly shown this in a paper which appeared a year before our work was published. His admirable studies, buried in an obscure journal, have not received the attention they deserve. In every instance in which we succeeded in separating the pancreas permanently from the intestine extreme atrophy of the gland occurred. Absence of marked atrophy and sclerosis as well as the good absorption of food prove that Lombroso, Niemann, Flecksеder, and other experimenters did not shut out all the pancreatic juice from the intestine.

Disease of the pancreas is relatively common, but disease of the pancreas with total exclusion of the pancreatic juice from the intestine is rare. There are scarcely two dozen cases in the literature in which the symptoms noted in our dogs, after total occlusion of the pancreatic ducts, were present.

In the clinical study of pancreatic disease it will be important to recognize, if possible, a diminution of pancreatic secretion as well as its total suppression.

Our experiments on dogs showed that the disturbance in absorption is slight when a small amount of functionating pancreas is left in connection with the intestine. In one dog Dr. Murphy separated the entire pancreas from the duodenum except for a wedge-shaped piece 1 cm. in length in the centre of which was the main pancreatic duct. The dog recovered rapidly from the operation. When fed on meat he had only one stool of moderate size daily. There was no fat visible on naked eye examination and no fat-droplets were seen with the microscope. The feces usually contained quite a large number of muscle fibers, with striations well preserved. The animal lost weight rapidly until fresh pancreas was added to his food. The operation was performed on March 16, 1910. The stools did not become fatty until the following November. The dog died on December 1, and the portion of pancreas that had been left connected with the intestine at the operation was reduced to a small strand of dense fibrous tissue. In another animal a small portion of the pancreas remained functionating after the operation. The stools were rather large, but well formed. A good many muscle fibers were present in the feces, but no apparent excess of fat. At the autopsy there was found a nodule of pancreatic tissue about 2 cm. in size, which contained acini and islands of Langerhans. Dr. Spooner demonstrated the presence of trypsin in the duodenal contents. In both of these animals the decreased

[9] Trans. Assoc. Amer. Phys., 1909, xxiv, 266.

[10] Medizinisch-Naturwissenschaftliches Archiv, 1908, i, 161.

pancreatic secretion was recognized by the presence of many muscle fibers in the stool, not by any excess of fat.

In the clinical study of cases of suspected pancreatic disease it is helpful to use the test diet of Adolf Schmidt. I have used it in my metabolism studies on patients during the past four years as well as in the routine examination of patients presenting symptoms of intestinal disease. This standard diet contains a very small amount of waste material. This is an important matter when a careful examination of the feces is to be made for the presence of undigested ingredients of the food. I have had no difficulty in inducing patients to follow this diet for the required period of three days. Sometimes, however, patients have refused to take the entire quantity of food prepared for each meal. Instead of following the original plan of giving five meals daily I have usually given the total amount of food in three meals. If this standard diet is used the results of absorption studies, as well as of the simpler clinical examinations, made by different investigators can be readily compared. Therein lies the great advantage of the Schmidt test-diet over similar ones that might readily be devised.

The form of test diet I have used is that given in the English translation of Schmidt's *Test Diet in Intestinal Diseases*, Philadelphia, 1906. It consists of "1.5 liters milk, 100 grams zwieback, 2 eggs, 50 grams butter, 125 grams beef, 190 grams potatoes, and gruel of 80 grams oatmeal. It contains about 102 grams albumin, 111 grams fat, 191 grams carbohydrates, or a total of 2234 calories."

In the morning: 0.5 liter milk (or, if milk does not agree, 0.5 liter cocoa prepared from 20 grams cocoa powder, 10 grams sugar, 400 grams water and 100 grams milk) and 50 grams zwieback.

In the forenoon: 0.5 liter oatmeal gruel (made from 40 grams oatmeal, 10 grams butter, 200 c.c. milk, 300 c.c. water, 1 egg; strained).

At noon: 125 grams chopped beef (raw weight), broiled rare with 20 grams of butter, so that the interior will still remain raw, and 250 grams potato broth (made of 190 grams mashed potatoes, 100 c.c. milk, and 10 grams butter).

In the afternoon: As in the morning.

In the evening: As in the forenoon.

In the recognization of severe pancreatic disease there is no single symptom of greater significance than bulkiness of the stools. This is a diagnostic sign to which Oser,[11] Musser,[12] and others have called attention. Much information can often be gained from the weight of the dried stools, and this can be ascertained even when facilities are not available for exact chemical analyses. All that is necessary in addition to scales for weighing is a water bath and a ventilating hood. With pancreatic juice absent from the intestine,

[11] Die deutsch. Klinik, Berlin, 1901, v, 165.
[12] Trans. Assoc. Amer. Phys., 1906, xxi, 346.

not only are the stools voluminous, but the dried residue is much in excess of the normal.

In a series of 6 healthy individuals placed on the test diet for three days, Schmidt[13] found the average weight of the dried feces to be 54.3 grams. The maximum was 62 grams and the minimum 45 grams.[14] I found in a case of obstructive jaundice associated with malignant disease of the pancreas that the weight of the dried feces was 419 grams in one metabolism period of three days, and 355 grams in another. In a patient with chronic fatty diarrhea and glycosuria without icterus the feces weighed 438 grams.

The increase in weight of the feces which results from shutting off the pancreatic juice from the intestine was well shown in our animal experiments. In a preliminary absorption test with the dog in normal condition the weight of the dried food in a period of three days was 624 grams, and the weight of the feces 140.4 grams. In a metabolism experiment of the same duration begun five days after separating the pancreas from the duodenum the weight of the dried food was reduced to 416 grams and that of the feces increased to 302.7 grams.

In none of the cases studied by Schmidt[15] was such a marked increase in weight of the feces observed as in our 2 cases of pancreatic disease. The average weight of the feces in 5 cases of "fermentative dyspepsia" reported by him was 127.4 grams; the average in "gastrogenous diarrhea" with achylia was 98.9 grams. His highest figures were in obstruction of the common bile duct, where the average weight was 175.6 grams, and the maximum 215.4 grams. There are no observations on cases of obstruction of the pancreatic ducts given by Schmidt. It seems to me that the possibility of shutting off the pancreatic secretion by an obstruction in the lower part of the common bile duct should be recognized. This may be the explanation of the heavy weight of the feces in 2 of his cases. It would be interesting to know if an obstruction high up in the common bile duct is associated with less disturbance of assimilation than one at the diverticulum of Vater. Unfortunately we have no information on this point.

Macroscopic Examination of the Feces. The light color of the feces is the most important sign of pancreatic disease brought out by the naked eye examination. This is due to the presence of fat, and if the amount of fat is large the stools become almost white. As the stools in icterus are also fatty, it may be necessary to make use of Schmidt's corrosive sublimate test for bile pigment in order to make sure that the pale color of the stools is not due in part to absence of hydrobilirubin. If fat crystals are present in large numbers they give to the feces a metallic lustre like that of

[13] Die Faeces des Menschen, Dritte Auflage, Berlin, 1910, p. 17.

[14] These figures of Schmidt are based on his original test diet, number II, which contains 1½ eggs and 20 grams more of sugar and 30 grams less of butter than the diet I employed.

[15] Loc. cit.

aluminum. When large amounts of fat were given to our dogs with obstructed pancreatic ducts they passed yellow masses of pure fat which looked like melted butter. I have seen only one patient whose dejections contained similar collections of macroscopic fat. With a diet rich in fat, Tileston[16] found masses of fat frequently in the stools of pancreatic disease. It should be borne in mind that fatty stools also occur in other conditions, chief of which are jaundice, already mentioned, diseases of the intestinal wall, and tabes mesenterica. Bits of muscle tissue, large enough to be easily recognized on inspection of the stools, were not found in our cases, and they were rarely seen in the feces of dogs after shutting out the pancreatic juice from the intestine.

Microscopic Examination of the Feces. The fat appears in the form of droplets, needle-crystals, and as structureless plates or flakes. The most trustworthy sign of the lack of pancreatic juice in the intestine is the presence of large numbers of yellow muscle fibers with sharp edges and with striations well preserved. They may be so numerous as to cover the entire field of the microscope when a low power is used.

To the pathological condition characterized by the presence of a large number of muscle fibers in the stool, Ehrmann[17] has recently given the name creatorrhea. Although a small number of undigested muscle fibers may be present in the stools in other conditions, especially in diarrhea, a well marked creatorrhea has never been observed in cases in which pancreatic insufficiency has been definitely excluded. The presence of numerous muscle fibers in the stools was recognized by Friedreich nearly forty years ago to be a valuable diagnostic sign of pancreatic disease.

Absorption of Fat and Nitrogen. In our dogs, as I have already stated, we found that shutting off all the pancreatic juice produced a great diminution in the absorption of both nitrogen and fat. This is shown in the following table:

Table I.

		Absorption in per cent. of N.	Fat.	Notes.
Dog II.	Experiment 1	22.2	11.3	Pancreas separated from duodenum.
"	" 2	62.1	48.5	Pankreon given.
Dog III.	Experiment 1	88.5	92.2	Before operation.
"	" 2	23.7	10.0	After excluding pancreatic secretion from intestine.
Dog IV.	Experiment 1	92.4	91.4	Before operation.
"	" 2	31.7	44.6	After excluding pancreatic secretion from intestine.
"	Experiment 3	47.8	63.4	
"	" 4	31.4	76.6	
Dog V.	Experiment 1	32.1	31.0	After excluding pancreatic secretion from intestine.
"	" 2	61.7	4.8	
"	" 3	42.4	20.1	
"	" 4	56.0	44.0	Holadin given.

[16] Albany Med. Ann., 1909, xxx, 619.

[17] Zeitsch. f. klin. Med., 1910, lxix, 331.

The clinical study of the metabolism of man in disease began with Friedrich Müller's[18] researches on icterus, published in 1887. In 3 cases of pancreatic disease he determined the amount and composition of the fecal fat. He concluded that the pancreatic juice could be excluded from the intestine without producing any quantitative change in the fecal fat. Autopsies were held in 2 of his cases. At that time it was not known that the human pancreas is regularly provided with two ducts. In the protocols no mention is made of the duct of Santorini. The entrance of pancreatic juice into the intestine through the accessory duct would explain Müller's findings. I analyzed the intestinal contents obtained at autopsy in a case of adenocarcinoma of the head of the pancreas, in which the duct of Wirsung was obliterated, but the duct of Santorini was patent. There was also obstruction of the common bile duct. The feces were not bulky and there was only 28.8 per cent. of fat in the dried residue.

In a number of cases of pancreatic disease metabolism studies have shown a great interference with the absorption of fat and nitrogen. Morrison and I made a metabolism experiment on a patient presenting the typical symptoms of total obstruction of the pancreatic ducts. There was no jaundice. It was found (Table II) that 58.9 per cent. of the fat of the food was excreted in the feces. The percentage of nitrogen unabsorbed was 50.9 per cent. Normally not over 5 or 10 per cent. of the fat or nitrogen of the food is lost in the feces.

TABLE II.

McC. Three days' experiment, October 20 to 22, 1908.
Weight of dried food 1297.5 grams. (Schmidt test diet.)
Weight of dried feces 438.0 grams.
Percentage of fat in food, 35.16; amount, 456.2 grams.
Percentage of fat in feces, 61.3; amount, 268.5 grams.
Percentage of nitrogen in food, 3.86; amount, 50.08 grams.
Percentage of nitrogen in feces, 5.82; amount, 25.49 grams.
Fat unabsorbed, 58.9 per cent.
Nitrogen unabsorbed, 50.9 per cent.

In a metabolism experiment on a patient with cancer of the pancreas and obstructive jaundice, Spooner and I found that 79.9 per cent. of the fat of the food was excreted in the feces and 34.8 per cent. of the nitrogen.

Vaughan Harley[19] reported a case of probable obstruction of the pancreatic ducts without jaundice, in which there was a fat loss of 73.1 per cent. In a case of cirrhosis and atrophy of the pancreas, combined with cirrhosis of the liver, Weintraud[20] found a fat loss

[18] Loc. cit.
[19] Jour. Path. and Bact., 1895, iii, 245.
[20] Die Heilkunde, 1898, iii, 68.

aluminum. When large amounts of fat were given to our dogs with obstructed pancreatic ducts they passed yellow masses of pure fat which looked like melted butter. I have seen only one patient whose dejections contained similar collections of macroscopic fat. With a diet rich in fat, Tileston[16] found masses of fat frequently in the stools of pancreatic disease. It should be borne in mind that fatty stools also occur in other conditions, chief of which are jaundice, already mentioned, diseases of the intestinal wall, and tabes mesenterica. Bits of muscle tissue, large enough to be easily recognized on inspection of the stools, were not found in our cases, and they were rarely seen in the feces of dogs after shutting out the pancreatic juice from the intestine.

Microscopic Examination of the Feces. The fat appears in the form of droplets, needle-crystals, and as structureless plates or flakes. The most trustworthy sign of the lack of pancreatic juice in the intestine is the presence of large numbers of yellow muscle fibers with sharp edges and with striations well preserved. They may be so numerous as to cover the entire field of the microscope when a low power is used.

To the pathological condition characterized by the presence of a large number of muscle fibers in the stool, Ehrmann[17] has recently given the name creatorrhea. Although a small number of undigested muscle fibers may be present in the stools in other conditions, especially in diarrhea, a well marked creatorrhea has never been observed in cases in which pancreatic insufficiency has been definitely excluded. The presence of numerous muscle fibers in the stools was recognized by Friedreich nearly forty years ago to be a valuable diagnostic sign of pancreatic disease.

Absorption of Fat and Nitrogen. In our dogs, as I have already stated, we found that shutting off all the pancreatic juice produced a great diminution in the absorption of both nitrogen and fat. This is shown in the following table:

Table I.

		Absorption in per cent. of		
		N.	Fat.	Notes.
Dog II.	Experiment 1	22.2	11.3	Pancreas separated from duodenum.
"	" 2	62.1	48.5	Pankreon given.
Dog III.	Experiment 1	88.5	92.2	Before operation.
"	" 2	23.7	10.0	After excluding pancreatic secretion from intestine.
Dog IV.	Experiment 1	92.4	91.4	Before operation.
"	" 2	31.7	44.6	After excluding pancreatic secretion from intestine.
"	Experiment 3	47.8	63.4	
"	" 4	31.4	76.6	
Dog V.	Experiment 1	32.1	31.0	After excluding pancreatic secretion from intestine.
"	" 2	61.7	4.8	
"	" 3	42.4	20.1	
"	" 4	56.0	44.0	Holadin given.

[16] Albany Med. Ann., 1909, xxx, 619.

[17] Zeitsch. f. klin. Med., 1910, lxix, 331.

The clinical study of the metabolism of man in disease began with Friedrich Müller's[18] researches on icterus, published in 1887. In 3 cases of pancreatic disease he determined the amount and composition of the fecal fat. He concluded that the pancreatic juice could be excluded from the intestine without producing any quantitative change in the fecal fat. Autopsies were held in 2 of his cases. At that time it was not known that the human pancreas is regularly provided with two ducts. In the protocols no mention is made of the duct of Santorini. The entrance of pancreatic juice into the intestine through the accessory duct would explain Müller's findings. I analyzed the intestinal contents obtained at autopsy in a case of adenocarcinoma of the head of the pancreas, in which the duct of Wirsung was obliterated, but the duct of Santorini was patent. There was also obstruction of the common bile duct. The feces were not bulky and there was only 28.8 per cent. of fat in the dried residue.

In a number of cases of pancreatic disease metabolism studies have shown a great interference with the absorption of fat and nitrogen. Morrison and I made a metabolism experiment on a patient presenting the typical symptoms of total obstruction of the pancreatic ducts. There was no jaundice. It was found (Table II) that 58.9 per cent. of the fat of the food was excreted in the feces. The percentage of nitrogen unabsorbed was 50.9 per cent. Normally not over 5 or 10 per cent. of the fat or nitrogen of the food is lost in the feces.

TABLE II.

McC. Three days' experiment, October 20 to 22, 1908.
Weight of dried food 1297.5 grams. (Schmidt test diet.)
Weight of dried feces 438.0 grams.
Percentage of fat in food, 35.16; amount, 456.2 grams.
Percentage of fat in feces, 61.3; amount, 268.5 grams.
Percentage of nitrogen in food, 3.86; amount, 50.08 grams.
Percentage of nitrogen in feces, 5.82; amount, 25.49 grams.
Fat unabsorbed, 58.9 per cent.
Nitrogen unabsorbed, 50.9 per cent.

In a metabolism experiment on a patient with cancer of the pancreas and obstructive jaundice, Spooner and I found that 79.9 per cent. of the fat of the food was excreted in the feces and 34.8 per cent. of the nitrogen.

Vaughan Harley[19] reported a case of probable obstruction of the pancreatic ducts without jaundice, in which there was a fat loss of 73.1 per cent. In a case of cirrhosis and atrophy of the pancreas, combined with cirrhosis of the liver, Weintraud[20] found a fat loss

[18] Loc. cit.
[19] Jour. Path. and Bact., 1895, iii, 245.
[20] Die Heilkunde, 1898, iii, 68.

of 25.2 per cent.; Deucher,[21] in cancer of the pancreas, found fat losses of 82.9 per cent. and 52.6 per cent.; Brugsch and König,[22] in a case of abscess of the pancreas, 59.7 per cent. (absorption experiment of only one day's duration). Glaessner and Siegel,[23] in a case of atrophy of the pancreas due to a calculus, found a fat loss of 56.1 per cent.; Gigon,[24] in a case of pancreatic calculi with obstruction of the ducts, a maximum fat loss of 47.4 per cent. and a minimum of 13.5 per cent.; Ehrmann,[25] in atrophy of the pancreas 50.2 per cent.; Tileston,[26] in 5 cases of cancer of the pancreas with icterus, fat losses of 75.6 per cent., 68 per cent., 52.6 per cent., 45.6 per cent., 49.1 per cent.

In Harley's case there was a nitrogen loss of 40 per cent.; Weintraud found a nitrogen loss of 60.6 per cent.; Deucher, 29.6 per cent. in one case and 19 per cent. in the other. Glaessner and Siegel, 41.5 per cent.; Gigon, 24.7 per cent.; and Ehrmann, 42.8 per cent.; Tileston, in 3 cases, 19.8 per cent., 14.5 per cent., and 21.1 per cent. Brugsch[27] found an average fat loss of 45 per cent. in 3 cases of icterus, but the nitrogen loss averaged only 11 per cent. If 50 per cent. or more of the fat and 25 per cent. of the nitrogen of the food are recovered from the feces the conclusion is warranted that pancreatic insufficiency exists.

Composition of the Fecal Fat. Müller observed that the feces contained a larger percentage of unsplit fat, that is, of neutral fat, in his cases of pancreatic disease than in other conditions studied. Zoja[28] asserted that a low percentage of soaps was of diagnostic value. Fitz,[29] in 1903, collected 11 cases from the literature in which an analysis of the fecal fat had been made. While in health, from 20 to 30 per cent. is in the form of neutral fat, in 9 out of 11 cases of disease of the pancreas the percentage of neutral fat was increased.

Since 1904 I have made analyses of the fecal fat in 7 cases of undoubted pancreatic disease. The fat extractions were made according to Rosenfeld's[30] method. In the determinations of the neutral fat, fatty acids, and soaps, Fr. Müller's[31] procedure was followed. The results are given in the following table.

[21] Korrespondenz-Blatt f. Schweiz. Aerzte, 1898, xxviii, 321.
[22] Berl. klin. Woch., 1905, xlii, 1606.
[23] Ibid., 1904, xli, 440.
[24] Zeitsch. f. klin. Med., 1907, lxiii, 420.
[25] Loc. cit.
[26] Trans. Assoc. Amer. Phys., 1911, xxvi, 526.
[27] Zeitsch. f. exper. Path. u. Ther., 1909, vi, 326.
[28] Morgagni, 1899. Ref. in Centralbl. f. inn. Med., 1899, xx, 1261.
[29] Trans. Cong. Amer. Phys. and Surg., 1903, vi, 36.
[30] Zentralbl. f. inn. Med., 1900, xxi, 833.
[31] Loc. cit.

TABLE III.—Analyses of Feces in Disease of the Pancreas.

CASE I.—Mrs. H. Cancer of pancreas, with occlusion of pancreatic ducts; glycosuria; obstructive jaundice. Autopsy.

	Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
Stool of January 28	2.0	49.7	22.5	58.7	18.8
Stool of February 22	5.0	62.8	29.1	63.2	7.7

CASE II.—B. Cancer of pancreas; transitory glycosuria; obstructive jaundice. Diagnosis confirmed by operation.

Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
6.0	72.8	39.7	50.5	9.8

CASE III.—Mrs. C. Cancer of pancreas; shortly before death on October 29 stools became soft and fatty. Autopsy. Obstruction of duct of Wirsung; accessory duct not found; partial obstruction of common bile duct.

	Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
October 9. Small clay-colored stool. It did not look fatty .	4.29	52.5	37.1	37.3	25.6
First stool that looked fatty . .	3.0	63.3	14.0	30.9	55.1

CASE IV.—S. Cancer of head of pancreas; slight jaundice. Diagnosis confirmed by tissue removed at operation.

Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
4.8	66.1	30.7	44.8	24.5

CASE V.—M. Cancer of pancreas; duct of Wirsung obliterated; duct of Santorini patent; partial occlusion of the common bile duct.

Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
28.8	3.9	18.2	77.9

CASE VI.—McC. Clinical diagnosis: Obstruction of pancreatic ducts. No autopsy.

Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
5.8	61.3	56.6	37.4	6.0

CASE VII.—G. Cancer of pancreas; complete occlusion of common bile duct; primary cancer of stomach. Operation.

Per cent. of nitrogen in feces.	Per cent. of fat.	Per cent. of neutral fat.	Per cent. of fatty acids.	Per cent. of soaps.
4.3	70.4	41.8	37.5	20.7

In all but one of these cases steatorrhea occurred. The percentage of fat ranged from 28.8 to 72.8, while normally the feces contain less than 25 per cent. In 4 of the 7 cases there was an increase in the neutral fat, but not sufficiently great to be of distinct diagnostic value. A very low percentage of soaps was found in 3 of the 7 cases.[32]

It is evident from these analyses that additional methods of examination must be used in order to make a positive diagnosis of pancreatic disease.

Effect of Administering Pancreas. The feeding of raw pancreas and pancreatic preparations causes an increased absorption of fat and nitrogen when there is a lack of pancreatic juice in the intestine. In our dogs with pancreatic juice absent from the intestine the feeding of fresh pancreas was followed by a great decrease in the loss of fat and nitrogen. Pancreatic preparations produced a less marked improvement in absorption, but in one experiment the addition of pankreon to the food reduced the fat loss from 88.7 per cent. to 51.5 per cent., and the nitrogen loss from 77.8 to 47.9 per cent.

It has been suggested by von Noorden, Fitz, and others, that in cases of suspected pancreatic disease the administration of raw pancreas or pancreatic extracts would be of diagnostic value. In a case of fatty diarrhea, apparently not due to disease of the pancreas, Morrison and I found in a five days' metabolism experiment a fat loss of 23.4 per cent., and a nitrogen loss of 16 per cent. Pankreon was given in large doses for a second period of four days, during which the fat loss was 25.7 per cent., and the nitrogen loss 15.3 per cent. These figures show that the pankreon had no effect on the absorption of food, and hence the experiment supports the view that the fatty diarrhea was not of pancreatic origin.

The results of absorption experiments made by a number of investigators have been collected by Tileston.[33] They show that pancreas and pancreatic preparations often decrease greatly the loss of nitrogen and fat in the feces. Sometimes, however, the effect of pancreatic preparations is so slight that it cannot be recognized unless an absorption experiment is performed.

A number of functional tests for the recognition of pancreatic insufficiency have been employed during recent years, and methods devised for demonstrating the enzymes of the pancreas in the feces, gastric contents, and urine.

Glutoid Capsule Test. This was introduced by Sahli[34] in 1897. Gelatine capsules containing salol or iodoform are hardened

[32] In dogs the fats were as well split after shutting out the pancreatic secretion as they were in normal dogs, and the percentage of soaps was not decreased (Pratt, Lamson, and Marks, Trans. Assoc. Amer. Phys., 1909, xxiv, 266).

[33] Trans. Assoc. Amer. Phys., 1911, xxvi, 537.

[34] Deutsch. med. Woch., 1897, xxiii, 6; Deutsch. Arch. f. klin. Med., 1898, lxi, 475.

in formalin. This renders them resistant to gastric digestion, but they are dissolved readily by the pancreatic juice. The capsules I used contained salol, which is broken down in the intestine and excreted in the urine as salicyluric acid. Its presence is recognized by the violet color produced by adding to the urine a few drops of a solution of ferric chloride. Normally the reaction is obtained within five hours. The test would probably have been more widely used if Sahli had disclosed his method of preparing the capsules. They are made and sold by Fr. Hansmann, St. Gallen, Switzerland. My observations are based on tests made with the original capsules. An attempt to make glutoid capsules in our laboratory by placing gelatine capsules in 10 per cent. formalin for varying lengths of time ended in failure. I tested the imported capsules in artificial digestive fluids, and confirmed the claim of Sahli that they would resist gastric digestion and yet dissolve readily in pancreatic juice. Sailer[35] has found that satisfactory glutoid capsules can be made by immersing ordinary gelatine capsules in pure formalin for three minutes.

The test has few friends, and does not seem to be often employed at the present time. Schmidt's pupil, Wallenfang,[36] found the reaction delayed in 4 out of 8 healthy individuals. Schmidt says that it is of negative value, for if the reaction occurs within the normal time limit he holds that pancreatic disease can be definitely excluded. This statement, however, cannot be accepted, as the following observation shows. On February 22 I gave Mrs. H. two glutoid capsules, each containing 0.5 grams of salol. They were administered with an Ewald breakfast at 8 A.M. Urine voided at 12 o'clock contained salicyluric acid. The patient died on March 5, and a cancer of the head of the pancreas was found apparently occluding both ducts. If there is motor insufficiency of the stomach the test may be retarded. In one of my patients in whom a gastro-enterostomy had been performed the reaction was delayed many hours. Operation revealed a normal pancreas. The stools were negative. Attention has been called by Fromme[37] to the importance of ruling out gastric stasis in cases in which the glutoid capsule test indicates pancreatic disease.

When there is total absence of pancreatic juice from the intestine it is possible that a delay in the reaction always occurs. In a dog with the pancreas completely separated from the duodenum the reaction after the administration of the capsule was delayed nearly twenty-four hours, and then only a trace of salicyluric acid was found in the urine. In another dog in which a small bit of the pancreas, 1 cm. in size, was left connected with the main pancreatic duct, the reaction was not definitely retarded. I used capsules of medium

[35] AMER. JOUR. MED. SCI., 1910, cxl, 330.
[36] Inaug. Dissert., Bonn, 1903, p. 18.
[37] Münch. med. Woch., 1901, xlviii, 591.

hardness, but Sahli[38] now states that capsules of maximum hardness should be employed for diagnostic purposes. I found the reaction delayed, however. with the softer capsule in a case in which the presence of trypsin was demonstrated in the gastric contents after an oil breakfast.

Schmidt's Cell Nuclei Test. The observation made by Schmidt,[39] that cell nuclei are digested only by the pancreatic secretion, is the physiological basis of the test. The method has been assailed on theoretical as well as on practical grounds. Brugsch[40] and his pupil Hesse[41] have been the chief opponents of the method, but they have failed to prove that it is untrustworthy, and Schmidt's assertion that the gastric juice does not act upon cell nuclei seems to be true. Strauch,[42] working in Abderhalden's laboratory, showed that pure pancreatic juice completely dissolved the cell nuclei in six to eight hours, pure intestinal juice (erepsin) and pure gastric juice, on the contrary, did not digest them.

I found in a dog with complete pancreatic achylia, produced by separating the pancreas from the duodenum, that the cell nuclei were not digested. The gastric juice was normal, and there was no disease of the intestine. Thus clear evidence was presented by this experiment that the normal secretions of stomach and intestine were unable to digest the cell nuclei.

Raw beef containing a fair amount of fibrous tissue is cut into cubes measuring about 0.5 cm. in size. These are hardened in alcohol, and placed in small bags made of silk gauze. They should be immersed in water for several hours before using. The bags are recovered from the stools, and the meat cubes examined for the presence of nuclei after paraffin sections have been prepared. The test is positive if the nuclei are preserved and take the stain, negative if the nuclei are digested. Einhorn[43] has used thymus gland instead of beef. This modification appears to be a distinct improvement, but I have had no personal experience with it.

Recently Kashiwado,[44] a pupil of Schmidt, has simplified the nucleus test. By gastric digestion the nuclei of the thymus gland are isolated. The nuclei are then stained with hematoxylin, and a powder prepared, composed of equal parts of lycopodium and nuclei. Two capsules, each containing 0.25 gram of the mixture, are administered after dinner or supper. If the nuclei are not digested they are easily recognized in the stools.

I have not observed a definite case of pancreatic insufficiency in which the nucleus test was negative. The value of the test is

[38] Diagnostic Methods, second English edition, Philadelphia, 1911 p. 606.
[39] Verhand. d. Kong. f. inn. Med., 1904, xxi, 335.
[40] Deutsch. med. Woch., 1909, xxxv, 2307; Zeitsch. f. exper. Path. u. Ther., 1909, vi, 326.
[41] Zeitsch. f. exper. Path. u. Ther., 1909, vii, 91; Deutsch. med. Woch., 1910, xxxvi, 121.
[42] Deutsch. Arch. f. klin. Med., 1910, ci, 128.
[43] Arch. f. Verdauungskrank., 1907, xiii, 475.
[44] Deutsch. Arch. f. klin. Med., 1911, civ, 584.

impaired by the fact that the meat cubes must remain in the intestine not less than six nor more than thirty hours. If the period is too short the nuclei are undigested by normal pancreatic juice. Putrefaction may cause the disappearance of the nuclei if the meat cubes remain more than a day in the intestine. In one of my cases the silk bags were recovered in the feces five days after they were taken into the stomach.

The preservation of the nuclei, with the test properly carried out, does not necessarily imply complete absence of the pancreatic secretion. In a case of fatty diarrhea with achylia gastrica the nuclei were not digested, but Spooner and I demonstrated trypsin in the stomach by Volhard's method. If with the nuclei test one can recognize cases in which there is a deficient secretion of pancreatic juice, the value of the method will not be diminished but enhanced. As already stated, there are few cases of pancreatic disease in which total absence of pancreatic secretion occurs, and these are readily diagnosticated.

In 1906 Schmidt[45] described cases in which he maintained there was functional pancreatic achylia. I have seen cases of the type he described, but I believe that, as in the one just mentioned, there is a deficiency of the pancreatic juice (hypochylia) rather than total suppression of the secretion. The absorption of fat and nitrogen may be so good that the stools present no suggestion of pancreatic disease and yet the cell nuclei may remian undigested as in a case reported by the late Dr. Steele,[46] of Philadelphia. Three times the test was repeated, and each time the cell nuclei were found intact. In the light of present knowledge it seems probable that this was an instance of functional pancreatic hypochylia. This view is strengthened by the fact that there was an absence of gastric secretion in his case.

Demonstration of Trypsin in the Stools. *The Serum Plate Method.* Müller and Schlect[47] found that trypsin would act upon the surface of a serum agar plate, producing small depressions. They demonstrated by this method the regular occurrence of trypsin in normal feces. The plates were kept at a temperature of 50° or 60° C., so that bacterial action was prevented. In several cases of primary and secondary disease of the pancreas trypsin was absent from the feces or greatly diminished. A number of investigators have found this method of value. It yielded positive results in 5 out of 6 cases of pancreatic disease examined by M. Hirchberg.[48]

The Casein Method. Casein in alkaline solution is precipitated by acidifying with dilute acetic acid. When the casein is digested by trypsin the addition of acetic acid produces no clouding of the solution. This is the basis of a method introduced by Gross[49] for

[45] Deutsch. Arch. f. klin. Med., 1906, lxxxvii, 456.
[46] Trans. Assoc. Amer. Phys., 1906, xxi, 346.
[47] Münch. med. Woch., 1908, lv, 225.
[48] Deutsch. med. Woch., 1910, xxxvi, 1892.
[49] Arch. f. exper. Path. u. Pharm., 1907, lviii, 157; Deutsch. med. Woch., 1909, xxxv, 1706.

detecting the presence of trypsin. More than 200 stools were examined by him, and in all cases in which disease of the pancreas could be excluded a protein splitting ferment was present in the feces. A modification of Gross's method has been used by Dr. Spooner in our laboratory for estimating the amount of trypsin present in the feces. In one of our dogs with the pancreatic juice excluded from the intestine there was no splitting of the casein by the feces. This would indicate that erepsin was not present in sufficient amount normally to act upon the casein. The possibility that there was a diminished production of erepsin in the intestine of our dog, however, cannot be denied, although it seems improbable. Brugsch and Masuda[50] have concluded from their investigations that the strong splitting of casein produced by fecal extracts cannot be attributed to erepsin. Spooner and I, in a recent case of cancer of the pancreas, found that the power of the feces to digest casein was entirely lost. In a case of fatty diarrhea, probably due to pancreatic hypochylia, the amount of trypsin in the feces was greatly reduced. In this case the cell nuclei were not digested in Schmidt's beef-cubes, and after the administration of Sahli's glutoid capsules no reaction was obtained in the urine even at the end of twenty-four hours. That an absence of trypsin in the feces always indicates disease of the pancreas is doubtful. No trypsin could be demonstrated in the feces of one of the workers in our laboratory. Four tests were made during a period of ten weeks. He presented no symptoms of disease.

Demonstration of Trypsin in the Stomach Contents. Boldyreff,[51] in Pawlow's Institute made the important discovery that the feeding of a large amount of olive oil to dogs caused the regurgitation of pancreatic juice and bile from the duodenum into the stomach. Volhard[52] and his pupil Faubel[53] were the first to use this method in the clinic. A breakfast, consisting of 200 c.c. of pure olive oil is given, or in place of the oil 250 c.c. of cream may be used.

As trypsin cannot be demonstrated in a strongly acid gastric juice, half a teaspoonful of magnesia should be given before breakfast and twenty minutes later, as suggested by Lewinski.[54] Some remove the stomach contents in half an hour, others at the end of forty-five minutes. Trypsin estimations can be made by Volhard's method or more easily by that of Gross.

Mahlenbrey[55] proved the presence of trypsin in the stomach contents of 38 out of 41 cases. This method has been utilized in

[50] Zeitsch. f. exper. Path. u. Ther., 1911, viii, 617.
[51] Zentralb. f. Physiol., 1904, xviii, 457; Zentralb. f. Phys. u. Path. des Stoffw., 1908, iii, 209.
[52] Münch. med. Woch., 1907, liv, 403. [53] Beitr. z. chem. Phys. u. Path., 1907, x, 35.
[54] Deutsch. med. Woch., 1908, xxxiv, 1582.
[55] Zentralb. f. ges. Phys. u. Path. des Stoffw., 1909, iv, 643, 689.

the diagnosis of pancreatic disease by Volhard,[56] Lewinski,[57] Ehrmann,[58] and M. Hirschberg.[59]

Spooner and I found trypsin in the stomach contents of a patient who had fatty diarrhea and achylia gastrica. The Schmidt nuclei test and the glutoid capsule test indicated pancreatic inactivity. Until the demonstration of trypsin in the oil breakfast the possibility of achylia pancreatica could not be excluded.

Demonstration of Trypsin by Duodenal Intubation. Attention should be called to the ingenius method of obtaining pancreatic juice directly from the duodenum devised by Einhorn.[60] A gold acorn-shaped bucket, the size of a bean, is swallowed. Attached to the bucket is a strong silk thread, the free end of which, passing out of the patient's mouth is fastened around his neck or to his clothes. After time has elapsed for the bucket to enter the duodenum a catheter is passed along the thread and so guided into the duoednum. By means of a syringe it is then possible to aspirate the duodenal contents through the catheter. Gross[61] has also invented a duodenal tube. Von Barth-Wehrenalp,[62] by the use of Einhorn's bucket without the aspiration catheter was able to obtain pancreatic secretion in 55 per cent. of the cases he examined. Junghans[63] demonstrated the presence of trypsin in 30 out of 50 cases. The bucket was retained by his patients the entire night, while von Barth-Wehrenalp removed it at the end of three hours. Junghans obtained no better results when the duodenal tubes of Einhorn and Gross were used. Einhorn[64] has improved his method. In place of the duodenal bucket he has devised a duodenal pump consisting of a small perforated metal capsule communicating with a long thin rubber tube. By means of a syringe connected with the rubber tube the duodenal contents are aspirated.

Diastase in the Feces. Within the last two years a new laboratory test has been employed by a few investigators in the diagnosis of pancreatic disease which is full of promise. This is the quantitative determination of the diastatic ferment in the feces and urine. Strasburger[65] was the first to show that diastase was normally present in the stools of adults. Its occurrence in the feces of children had long been known. Strasburger thought the starch-splitting enzyme was a product of the intestinal secretion. Its clinical significance was not realized until Wohlgemuth proved that the diastase of the feces came chiefly from the pancreas. The original method of diastasimetry is that of Roberts. The one chiefly

[56] Loc. cit. [57] Loc. cit. [58] Loc. cit. [59] Loc. cit.

[60] New York Med. Jour., 1908, lxxxvii, 1179; Arch. f. Verdauungskrank., 1909, xv, 727; Med. Rec., 1909, lxxvi, 595.

[61] New York Med. Jour., 1910, xci, 77; Jour. Amer. Med. Assoc., 1910, liv, 1365.

[62] Intern. Beit. z. Path. u. Ther. d. Ernährungstor., 1910, i, 530.

[63] Zentralb. f. Phys. u. Path. d. Stoffw., 1911, vi, 49.

[64] Med. Rec., 1910, lxxvii, 98; Jour. Amer. Med. Assoc., 1910, lv, 6.

[65] Deutsch. Archiv f. klin. Med., 1900, lxvii, 238, 531.

used at the present time was introduced by Wohlgemuth.[66] It has been modified by Wynhausen[67] and Hawk.[68] Other methods are those described by Salkowski, E. Müller,[69] and Durand.[70]

E. Müller, using his starch plates, found a very weak diastatic action of the stool in a case of complete occlusion of the ductus pancreaticus. Einrequez, Ambard, and Binet[71] noted an absence of diastase in the feces of 2 cases of cancer of the pancreas. Wynhausen[72] examined 4 cases of pancreatic disease (2 of cancer; 2 of hemorrhagic pancreatitis). In none of these were more than 30 diastase units in the stool, while normally an average of 500 units are found. Balint and Molnar[73] reported that in a case of cancer of the pancreas repeated examinations of the stool showed the total absence of diastase. Wynhausen,[74] in a more recent paper, states that in 12 cases of pancreatic disease confirmed by autopsy the method of Wohlgemuth yielded trustworthy results, not only in cancer of the pancreas, but in diffuse affections of the gland which did not involve the ducts.

Diastase in the Urine. The observation of Wohlgemuth[75] that the experimental occlusion of the main pancreatic duct in dogs is followed by a marked rise in the amount of diastase in the urine lead to the important discovery that in acute functional disturbances of the pancreas in man a similar increase in the diastase of the urine occurs. In 2 cases Wohlgemuth[76] obtained values of 625 and 1250, while the highest observed normally was 150 units. Hirschberg[77] found a large amount in 2 cases of acute pancreatitis, and Wynhausen in 2 cases of cancer of the pancreas. The increase is seen only in acute disease or at the onset of increased disturbance of function which may occur in a chronic disease.

Lipase in the Urine. Opie,[78] in 1902, reported the occurrence of a fat-splitting ferment in the urine of a case of acute hemorrhagic pancreatitis. His test is open to criticism, because the possibility cannot be denied that the lipolytic action he observed was due to bacteria. Hewlett[79] has clearly demonstrated, however, that lipase appears in the urine of dogs after obstruction of the pancreatic duct, and during acute pancreatitis experimentally produced.

In 2 cases of acute pancreatitis in which I examined the urine I could find no fat-splitting ferment. I used the same method as did Opie, but added toluol to check the development of bacteria. In the new edition of his work on the pancreas, published in 1910,

[66] Biochem. Zeitsch., 1908, ix, 1.
[67] Berl. klin. Woch., 1909, xlvi, 1406.
[68] Arch. Int. Med., 1911, viii, 417.
[69] Zentralb. f. inn. Med., 1908,xxix, 385.
[70] Arch. mal. app. digest., 1911, v, 76.
[71] Sem. Méd., 1909, xxix, 13.
[72] Berl. klin. Woch., 1910, lxvii, 478.
[73] Berl. klin. Woch., 1910, xlvii, 1623.
[74] Abstracted in Zentralb. f. inn. Med., 1911, xxxii, 818.
[75] Biochem. Zeitschr., 1909, xxx, 432.
[76] Berl. klin. Woch., 1910, xlvii, 92.
[77] Loc. cit.
[78] Johns Hopkins Hosp. Bull., 1902, xviii, 117.
[79] Jour. Med. Research, 1904, vi, 377.

Opie[80] records no additional cases either of his own or from the literature.

Ethereal Sulphates in the Urine. Absence of pancreatic juice diminishes intestinal putrefaction because bacteria break down proteins less easily than they do the end-products of pancreatic digestion. Hence the claim has been made that in pancreatic disease the ethereal sulphates in the urine are decreased or absent. In the urine of a normal dog on a meat diet, I found the ratio of ethereal to preformed sulphates was 1 to 9. In a dog with pancreatic juice absent from the intestine the ratio was 1 to 21.6 on one day, and 1 to 23.5 on the following day. Rosenberg,[81] after tying one or more of the pancreatic ducts in a dog found the ratio was 1 to 15.9. Gigon,[82] in the urine of a patient with pancreatic calculi obtained a ratio of 1 to 39.3, while normally it is about 1 to 10. Le Nobel,[83] in a case of pancreatic disease found "no conjugate sulphuric acid." There was no decrease in the ethereal sulphates in a case of pancreatic insufficiency studied by Tileston.[84]

Disturbance of the Internal Function of the Pancreas. All the functional tests described thus far in this paper have dealt with the enzymes of the external secretion, and the symptoms due to their absence from the intestine.

In addition there is the internal function which controls in some way, quite unknown, the normal destruction of sugar in the body. In disease of the pancreas the limit of assimilation for carbohydrates may be greatly lowered even when spontaneous glycosuria does not occur. In my dogs with atrophy of the pancreas this diminished tolerance was a constant symptom.

Alimentary Glycosuria. If a lowered limit of assimilation for sugar exists in patients with suspected pancreatic disease, it can be discovered by giving 100 grams of glucose and testing the urine for sugar during the following twenty-four hours. The solution of glucose may be made more palatable by the addition of coffee. It is better to give the sugar after a light breakfast rather than on a fasting stomach.

In a collection I have made of 37 cases of pancreatic disease, carefully studied by functional methods, spontaneous glycosuria occurred 6 times and alimentary glycosuria 4 times. Only 2 of the 10 cases were cancer.

It is important to make repeated examinations of the urine as transitory glycosuria is a symptom that is frequently overlooked.

Cammidge Test. This so-called pancreatic reaction[85] seems to deserve the discredit into which it is falling. I think Wohlgemuth[86]

[80] Diseases of the Pancreas, second edition, Philadelphia, 1910, p. 198.
[81] Pflüger's Archiv, 1898, lxx, 404.
[82] Zeitsch. f. klin. Med., 1907, lxiii, 420.
[83] Deutsch. Archiv f. klin. Med., 1888, xliii, 280.
[84] Trans. Assoc. Amer. Phys., 1911, xxvi, 522.
[85] Lancet, 1904, i, 782. Improved methods described in Brit. Med. Jour., 1906, i, 1150; Surg., Gyn., and Obstet., 1908, vi, 29.
[86] Berl. klin. Woch., 1910, xlvii, 92.

does not state it too strongly when he says that the Cammidge test is "geradezu wertlos." A test which may be positive in health and in a variety of diseases in which the pancreas is normal, and negative when the pancreas is extensively diseased certainly has little to commend it. This opinion is supported by the fact that in 2 dogs in which we produced progressive chronic inflammation of the pancreas by obstructing the ducts the Cammidge reaction was negative.

LOEWI'S TEST. After extirpation of the pancreas in dogs and cats, Loewi[87] produced dilatation of the pupil by the instillation of adrenalin. He attributes the dilatation to an increased excitability of the sympathetic nervous system. In man he found the reaction in a case of occlusion of the pancreatic ducts without glycosuria. He also obtained a similar mydriasis in 10 out of 18 diabetics, and Falta,[88] in 15 out of 36 cases of diabetes. Cords[89] examined 11 cases of diabetes and only 3 were positive. Bittorf[90] observed the reaction only twice among diabetics, and both of his patients were moribund at the time. In 3 dogs with extreme atrophy of the pancreas I found the test negative, and also in the case of a man who developed diabetes several years after an attack of hemorrhagic pancreatitis.

DIAGNOSIS OF ACUTE DISEASE OF THE PANCREAS. Until recently the functional tests have furnished little, if any, aid in the recognition of acute pancreatitis. I know of no case in which a serious interference with the absorption of fat and nitrogen has been shown. Stockton[91] has recently called attention to the slight disturbance of the fat digestion. I made an analysis in one case and found only 17.4 per cent. of fat in the dried stool; 50.3 per cent. was in the form of neutral fat, 21.6 per cent. as fatty acid, and 28.7 per cent. as soap. There was 5.8 per cent. of nitrogen.

Recent observations on the occurrence of large amounts of diastase in the urine in acute pancreatitis give foundation for the hope that a determination of the diastase in the urine may prove of great aid in the diagnosis.

DIAGNOSIS OF CHRONIC DISEASE OF THE PANCREAS. Pancreatic insufficiency, even of mild degree, can be recognized by the functional methods of diagnosis now available. At the present time no single sign or symptom can be accepted as pathognomonic of pancreatic disease, but by the use of a number of different tests the diagnosis can be made.

The functional tests have already thrown much light on the pathological physiology of the pancreas. Observations made with these tests indicate that diminished or altered secretion of the pancreas may occur without demonstrable anatomical changes in the organ.

[87] Arch. f. exper. Path. u. Pharm., 1909, lix, 83.
[88] Wien. klin. Woch., 1907, xx, 1559.
[89] Die Adrenalin Mydriasis und ihre diagnostische Bedeutung, Wiesbaden, 1911, p. 45.
[90] Zentralb. f. inn. Med., 1909, xxx, 33.
[91] Trans. Assoc. Amer. Phys., 1911, xxvi, 545.

Within the last few years much interest has been aroused in the diagnosis and surgical treatment of chronic pancreatitis. This has been chiefly due to the papers of Robson,[92] in England, and those of Deaver[93] and William Mayo[94] in this country.

Riedel,[95] as early as 1896, stated that in 3 out of a series of 122 cases of cholelithiasis the head of the pancreas was enlarged and very hard.

Many cases have been reported by surgeons during the last twelve years in which the diagnosis of chronic pancreatitis was made. Mayo Robson regards the condition as a clinical entity. He and his followers claim that obstruction of the common duct is frequently due to the pressure exerted by the swollen head of the pancreas.

Opie,[96] however, in his text-book refers to only 1 case in which occlusion of the common duct by the pancreas was demonstrated at autopsy. Our experiments on dogs show that extreme chronic pancreatitis and atrophy do not interfere with the health of the animal, provided a small amount of secreting tissue remains.

Among the cases reported by surgeons of the type of chronic pancreatitis described by Mayo Robson, I have found none in which the evidence was convincing that pancreatic insufficiency was present, or that the obstructive jaundice was due to pressure exerted by a swollen pancreas. In many cases the symptoms might equally well be attributed to chronic cholangitis. As Riedel[97] pointed out, the icterus associated with stone in the common duct is much more often due to inflammation of the duct than to mechanical obstruction produced by the stone.

It should be borne in mind that a hard pancreas is not necessarily a diseased pancreas. I know of cases in which the diagnosis of chronic pancreatitis was based on the hard feel of the pancreas at operation, and subsequently at autopsy a normal pancreas was found. It is a matter of common knowledge among pathologists that a normal pancreas may have a consistence of almost stony hardness. These facts are brought forward to emphasize the importance of coöperation between the surgeon, the clinical pathologist, and the pathological anatomist. If the cases which the surgeon at the operating table regards as chronic pancreatitis are examined with the aid of the functional methods of diagnosis, pancreatic insufficiency, if it exists, will be detected. Proof will then take the place of conjecture and knowledge of pancreatic disease will advance.

[92] Lancet, 1900, ii, 236; 1904, 861; Robson and Moynihan, Diseases of the Pancreas, Philadelphia, 1902, p. 147; Robson and Cammidge, The Pancreas: Its Surgery and Pathology, Philadelphia, 1907, p. 412.

[93] Amer. Jour. Med. Sci., 1903, cxxv, 187; Jour. Amer. Med. Assoc., 1911, lviii, 11; Amer. Med., 1904, vii, 465.

[94] Jour. Amer. Med. Assoc., 1908, l, 1161.

[95] Berl. klin. Woch., 1896, xxxiii, 2.

[96] Disease of the Pancreas, Philadelphia, second edition, 1910, p. 244.

[97] Loc. cit.

PELLAGRA IN ITS RELATION TO NEUROLOGY AND PSYCHIATRY.[1]

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Four years ago there were probably not half a dozen physicians in America who had given pellagra any serious thought, but today it attracts the attention, or should, of every American physician and is of especial interest to the internist, the hygienist, the dermatologist, the neurologist, and the alienist. Previous to 1907 only a few sporadic cases had been observed in this country when Searcy,[2] of Alabama, during this year, reported 88 cases observed in the State Insane Asylum. Last year there were estimated to be 5000 pellagrins in the United States,[3] while this year it is said there are 10,000, some alarmists putting the figure even much higher. The onset of many cases was undoubtedly some years previous to 1907, but the disease was not a known factor in this country until that year. Neither is the disease, as many suppose, confined to the Southern States. Over 200 cases have been reported from the State Insane Asylum at Peoria, Illinois, and I understand that a dozen cases have been diagnosticated at the Philadelphia General Hospital. There are probably but few large charity institutions in the United States in which there is not a case. The question as to how the disease spreads is a large one and has not been settled. It is not considered contagious.

The disease has been studied in this country mainly in institutions for the insane where some of the cases developed, but where most were admitted with pellagra in an advanced stage. The writer[4] published about a year ago the study of 55 non-institutional cases, and his work since has been chiefly confined to this class of cases. In the present paper, after a brief general description of the disease, it is proposed to take up the study of pellagra from a neurological and a psychiatrical viewpoint, to call attention to various symptoms under these headings in the analysis of 88 cases and to make some deductions therefrom.

Gastro-intestinal and Cutaneous Symptoms. The symptoms of pellagra should be described under four headings representing more or less four different symptom-complexes. First are the gastro-intestinal or alimentary symptoms. The extent of the alimentary canal from the lips to the anus is often inflamed and during the attack some portion will be affected, even if only mani-

[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, December 19, 1911.

[2] Jour. Amer. Med. Assoc., July 6, 1907, p. 37. [3] Amer. Jour. Insanity, January, 1911.

[4] Jour. Amer. Med. Assoc., January 28, 1911, p. 246.

fested by sore mouth. Stomatitis, nausea, vomiting, diarrhea and proctitis are common symptoms of the disease. Most writers have placed the cutaneous symptoms as the first manifestation of pellagra, but a careful review of early cases made by me brought out the fact that at least 80 per cent. gave a history of diarrhea or nausea and vomiting before cutaneous symptoms were noted. I believe if more accurate observations could be made and stomatitis included this percentage would be greatly increased.

The characteristics of the cutaneous lesions are that they are symmetrical, that the backs of the hands are always involved, usually at the beginning, that the lesions extend up the forearm on the extensor surfaces and have a tendency to become annular at the wrists and elbows. Lesions may also appear on the fore-

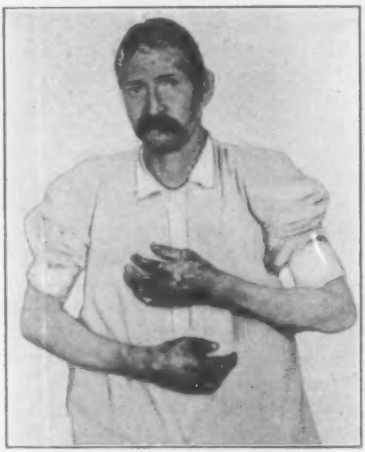

FIG. 1.—Cutaneous lesions of pellagra, showing symmetrical involvement of the backs of the hands and forehead.

head, cheeks, alæ nasi, chin, neck and dorsum of the feet. In the beginning they are usually erythematous in appearance, the skin quickly becoming rough and dark, often fissuring and sometimes sloughing. Bullæ filled with serum sometimes appear. Itching or burning may or may not accompany the skin lesions. As the lesions heal marked desquamation takes places. Accompanying the gastro-intestinal symptoms or the skin lesions, or following them shortly, are nervous manifestations and frequently mental symptoms. These will be taken up separately in this paper as we proceed. Among the general symptoms are loss of weight, moderate secondary anemia, malaise, and weakness. Females are more frequently affected than males and no age is exempt.

COURSE. Pellagra usually makes its appearance in the spring or summer. If the patient lives through the first attack there is a remission during the winter and a return of the symptoms the following spring or summer. Thus there is an acute or fulminating form in which the patient dies in from a few weeks to a few months and a chronic or recurrent form which may last a few or many years. The mortality during the first two years of the disease is over 50 per cent., recurring cases have been known to live fifteen or twenty years. In a few cases, hardly 10 per cent., recurrence does not appear and the patients are apparently cured.

LABORATORY FINDINGS. Neither stomach, fecal, blood or urinary examinations have thrown much light upon the study of pellagra. Absent hydrocholoric acid in the gastric juice is reported in many cases, but this is by no means constant. Ameba are frequently found in the stools but have no causative relation. A moderate and sometimes a severe secondary anemia is present. Wassermann reactions are negative. No especial study of the cerebrospinal fluid has been made. This should be done, as it may possibly throw some light upon the subject.

ETIOLOGY. The Italian school has generally accepted the theory that pellagra is caused by a toxin from spoiled maize. This theory has been largely discarded by American students of the disease and to my mind is disproved. Suffice it to say here that pellagra has occurred in localities where corn products were rarely eaten and in persons who stated that they never ate cornmeal bread. Cotton-seed oil, various bacteria, protozoa and fungi have been exploited as the cause, but none of these have been substantiated. Bass[5] recently stated that he has obtained, chiefly from the stools of pellagrins, cultures of bacteria which, when mixed with meal and water, and fed to chickens, gave a skin lesion said to resemble pellagra. We should certainly not accept this report until absolutely proved on the human subject. Sambon has endeavored to prove that pellagra is due to some product inoculated by the sand fly and lays stress upon its occurrence near streams. Two of my recent cases were in women, neither of whom lived within half a mile of a stream or creek, and both of whom had violent cases, although they practically never went near the stream, while those of the family whose occupation as farmers took them to the stream did not develop it. Beall[6] has made the same observation in a number of cases occurring in Texas.

The sun rays make the skin lesions worse, but seem to have no other relation, as lesions sometimes develop on the feet of those who wear shoes and stockings, and the lesions in those whose right hands are more exposed are equally severe on their left hands. Warm weather seems to have some special influence and the

[5] Jour. Amer. Med. Assoc., November 18, 1911, p. 1684.

[6] Ibid., p. 1683.

cases are better in the summer when a cool spell occurs. Bad personal hygiene, poor food and frail health undoubtedly add to susceptibility to pellagra.

FIG. 2.—Characteristic cutaneous lesion in which the skin has become rough and fissured.

PATHOLOGY. In regard to the pathology of pellagra, we shall have to be brief, and this may be just as well, for we know but little of its pathology. A review of the general pathology shows nothing specific. Harris,[7] in a study of the pathology of the nervous system, states that there may be noted changes in the chromophilic cells of the cerebral cortex and degeneration of the cells of Purkinje in the cerebellum. Cellular degeneration was noted in various parts of the cord, but no positive evidence of peripheral nerve alteration was found. Spiller,[8] in a study of the cord in 2 cases, concludes that pellagra does not produce a truly systemic disease of the central nervous system. He thinks the degeneration is caused by some toxic or infectious substance affecting all parts of the cerebrospinal axis, producing cellular degeneration and diffuse degeneration of nerve fibers in the posterior and anterolateral columns.

NERVOUS AND MENTAL SYMPTOMS. We shall now speak especially of the nervous and mental symptoms of pellagra. Your attention is called to the fact that a pellagrin may have nervous

[7] Trans. National Conference on Pellagra, Columbia, S. C., November 3 and 4, 1909, p. 86.
[8] AMER. JOUR. MED. SCI., January, 1911.

symptoms without definite mental ones, especially in the early stages of the disease. It is best not to follow the custom of intermingling the nervous and mental symptoms, but to segregate them as much as possible, although they may, and usually do, coexist. Thus, in the study of these symptoms in 88 cases we find that 100 per cent. showed nervous symptoms and 95 per cent. mental symptoms, the nervous manifestations usually appearing first. Several of the cases had been nervous for years, but their symptoms increased when pellagra developed.

Neurological Symptoms. Among the neurological symptoms we have restlessness in 84 per cent., insomnia in 88 per cent., muscular weakness in 92 per cent. of the 85 cases tested, and muscular wasting was noticed about in proportion to the loss of weight, which was practically constant. Local atrophies or dystrophies were not noticed. Vertigo was present in 76 per cent. of 81 cases. Headache was present in 60 per cent. In regard to sexual power the question was answered in only about one-third of the cases, and it was lost in 25 per cent. of these. Tremors were noted in 53 per cent. of the cases. The tremors chiefly involved the hands and tongue. Cramps were noted in 50 per cent. of the cases and were variously located in the abdomen, legs, arms, thighs and backs. Exophthalmos was noted in 3 per cent. of the cases and seemed to have no special reference to the disease. Of the more organic symptoms, anesthesia of areas of the cutaneous surface was noted in 20 per cent. of 69 cases tested. The mental condition of many of these cases precluded definite interpretation. Tenderness of the spine to percussion was noted in 20 per cent. of 54 cases tested. Contraction of the limbs was noted in 5 per cent. of the cases and was usually transient. Trophic disturbance excluding cutaneous lesions were noted in 13 per cent. of the cases and was chiefly manifested by roughening and thickening of the nails. Paralysis occurred in 7 per cent. of the cases, 3 of these showed paraplegia, 1 hemiplegia, 1 monoplegia and 1 paralysis of the sphincter ani. Rhomberg symptom was present in 57 per cent. of 66 cases tested. Ataxia was frequently present in severe cases but not numerically recorded. Knee-jerks were present in 88 per cent. of 74 cases tested, in 62 per cent. of these they were exaggerated on both sides, in 1 case they were exaggerated only on one side. In 9 of the 74 cases the knee-jerks were absent, in 7 they were decreased. Ankle clonus was not regularly tested, however, I have tested it in many cases which had exaggerated knee-jerks and found it not present. The same may be said of the Babinski phenomenon. The pupils in size were normal in 55 per cent. of the cases, contracted in 20 per cent., and dilated in 25 per cent. In only 2 of these cases were they noted to be unequal in size. The pupils reacted normally to light in 83 per cent. of 79 cases tested. Reaction to light was absent in 6 per cent. and sluggish in 11 per cent. Speech difficulty

occurred in 40 per cent. of the cases. In 2 cases aphasia was noted, in 6 mutism and in the rest speech was described as mumbling, slurring, or weak. Investigation of the special senses showed that smell was affected in 23 per cent. of the cases, in all of which it was diminished. Hearing was affected in 15 per cent., a diminution only being noted. Taste was diminished in about 50 per cent. of the cases, but this test was obscured by the almost constant and often severe stomatitis. Touch changes were noticed when the patients touched objects with their finger balls in 29 per cent. of the cases, being diminished in all except 2 cases in which it was increased. The only sight changes were errors of refraction. Neither diplopia nor photophobia were noticed.

Psychiatrical Symptoms. A study of the mental condition of these patients showed emotional irritability manifested either by excessive weeping or outbursts of temper in 53 per cent. of the cases. Depression was present in 84 per cent. of the cases and in about half of these the patients were said to have ceased laughing since the onset of the attack. Memory was distinctly poorer than usual in 74 per cent. of the cases. Delusions and hallucinations were present in about 20 per cent. of the cases. Most of the delusions were those of persecution and were unsystematized, and the hallucinations were the usual ones of sight and sound. These symptoms are much more common among institutional cases. Apprehension, varying from anxiety about their condition to delusions of impending danger, was present in 100 per cent. of the cases. Homicide was not attempted in any of these cases, but suicide was committed by 1, attempted by 2, and threatened by 6.

Nervous Syndrome. The nervous syndrome of the pellagrin may then be said to consist of restlessness, insomnia, muscular weakness and vertigo as almost constant symptoms, with headache, tremors, cramps, changes in the knee-jerks and pupil lay reflex, sway in station and slowness of speech occurring in about one-half of the cases, while areas of cutaneous anesthesia, loss of sexual power, tenderness of the spine, and diminution of smell and of finger touch are found in about one-fourth of the cases. Trophic disturbances, contraction of the extremities, ataxia and paralysis sometimes occur. Many mild or early cases only show restlessness, weakness, insomnia and vertigo, while all of the severe cases with which I am familiar show deep reflex, pupil and special sense changes before death.

Mental Syndrome. The mental syndrome of these non-institutional cases shows apprehension, depression, emotional irritability and failing memory as common symptoms, with delusions and hallucinations and suicidal tendencies not infrequent. The mental symptoms, except apprehension, may be absent in mild or chronic cases and severe cases may occasionally go on to

death without developing delusions or hallucinations. All of the severe cases show depression, emotional changes or failure of memory. The severe mental symptoms somewhat resemble melancholia, but they are usually accompanied by neurological signs not found in melancholia, the melancholia depression attitude is not often assumed, the agitation shown by wringing the hands is not seen and delusions of unworthiness are not present. Some of the mental states are said to resemble mania, but I have never seen the flight of ideas, the chaotic delusions, the changes of personality, the exaltation or the increased strength so common in acute mania.

In fact, neither the nervous nor mental syndrome of pellagra corresponds to any known nervous or mental disease, nor, indeed, do they hew closely enough to any one line to form a true clinical entity, but appear to be due to the action of some general toxin or organism. This opinion, as far as mental symptoms are concerned, agrees with that of most of the pellagrologists, who have studied the disease in insane asylums. I have not been able to find a previous attempt to more or less segregate the nervous from the mental symptoms. This attempt was thought justifiable after observing many cases of mild chronic pellagra for several years who did not show any real insane symptoms.

TREATMENT. Only a few words as to treatment will be mentioned in this paper. Urotropin has been used by me or at my suggestion in 20 odd cases and in all cases, with the exception of 2, who lived long enough to take the drug in doses of 10 grains four times a day for ten days either recovered from the attack or, as in 2 other cases, recovered all but their mental symptoms. One typical case has had no symptoms since 1909. A recent report by King and Crowell[9] seems to show the administration of salvarsan almost a specific. I have not yet tried this. I have certainly not been impressed with any other drug than hexamethylenamine. With the drug treatment as much nourishment as can be assimilated should be given and residence in a far Northern clime may be tried.

CONCLUSION. In conclusion I shall say that although there have been various small sums raised for the study of pellagra, and the next Congress will be asked for an appropriation of $50,000 for this purpose, and the New York Post-Graduate Laboratories propose to send workers into the field next spring and a small hospital for pellagrins has been opened in Georgia, the magnitude of the problem has not been appreciated. The disease threatens to be a national calamity, for it is both increasing in the Southern States and spreading North and West. No richer field for study may be found for medical investigators and no disease bears the same interest to workers in as many distinct lines as pellagra.

[9] Jour. Amer. Med. Assoc., November 18, 1911, p. 1687.

Money is needed, not to send small independent commissions into various sections, but to form a large central commission with organized branches all over the field. The problem will, of course, eventually be solved, but we are primarily a life saving profession, and every summer which is allowed to go by before it is solved means the death of many thousands of our citizens.

GASTRIC OR INTESTINAL HEMORRHAGE AS AN EARLY MANIFESTATION OF A GENERAL TOXEMIA.

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and
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Gastric or intestinal hemorrhage has been frequently observed to occur in the course of various pathological conditions. It is not the purpose of this paper to discuss the hemorrhages occurring with such infectious diseases as measles, scarlet fever, or variola, but those of purely septic or toxic origin. Dr. W. J. Mayo,[1] in a paper presented at the last meeting of the American Surgical Association makes the following statement: "Toxic erosion of the gastric mucosa is the usual cause of the gastric hemorrhages which accompany cirrhosis of the liver, splenic anemia, and certain disordered blood states." Henschen[2] refers to the occurrence of these erosions in tuberculosis, nephritis, brain disease and pneumonia, and says that the fact of their occurrence justifies the inquiry whether they are not dependent upon general instead of local conditions.

The writers of this paper will not enter deeply into a study of the etiology, but in presenting a few cases for your consideration, prefer to have this contribution considered as suggestive rather than conclusive.

Whether profuse gastric hemorrhage can occur without gross pathological lesion is a subject to which English surgeons and pathologists have in recent years given their attention. The term gastrotaxis has been applied to a condition in which free oozing of blood from the mucous membrane of the stomach occurs, and in which there is no evidence of ulceration of that organ nor other pathological process from which bleeding is likely to occur. Bolton,[3]

[1] Annals of Surgery, September, 1911, p. 313.
[2] Wien. medisin. Presse, 1902, No. 46.
[3] Brit. Med. Jour., May 21, 1910.

in discussing this condition states: "In severe anemias, in infective disease, in purpuric conditions, in toxemias associated with disease of the liver and kidneys it is a common experience to find the mucous membrane of the stomach intact when vomiting of blood has occurred during life." It is to the class of cases in which hemorrhage from the stomach or intestines occurs as the initial symptom, without pathological disorganization of the mucosa or the presence of an ulcerative process of any kind that we wish to call attention.

Singularly enough hemorrhage has occurred in the newborn much more frequently than in the adult. Our literature presents a great array of observations on this class of cases. It has been suggested that in many instances syphilis is responsible for this hemorrhagic condition in the newborn. That it is by no means a constant factor is generally admitted. Serious hemorrhages can occur, with perhaps no explanation for their occurrence. The following is an illustrative case.

E. S. was born October 27, 1905. Both of her parents are vigorous and free from any syphilitic taint. Dr. A. G. Doust delivered the child without instruments, and the labor was in every way perfectly normal. The child was apparently well until she was three days old. On that day she had two very profuse gastric hemorrhages, and one of us (Dr. Jacobson) was asked to see her with the attending physician. On the following day there were several discharges of blood by the bowels. In some of the bowel movements the blood appeared black, and in others it was of brighter color and profuse enough not only to saturate the napkins, but the bedding as well. Adrenalin was administered. The hemorrhage ceased after the fourth day, and the child recovered. In the six years which have elapsed she has had no sickness, and particularly no evidence of gastric or intestinal derangement. There are two other children in the family, both of whom are well, and there is no hemophilic tendency in any branch of the family. It would be difficult to assign a cause for the hemorrhage in this case. The child had no fever nor other evidence of a toxic condition. The fact that she so promptly recovered and has remained well since would seem to be conclusive that no serious pathological process existed at that time, and that the condition was probably dependent upon some temporary disturbance, which after all might have been toxic.

Our second case one of us (Dr. Jacobson) saw in consultation with Dr. McLennan at the Syracuse Hospital for Women and Children on May 26, 1905. This child was then two days old. She had been delivered after a protracted labor which lasted into the third day, by Dr. Sears, who was finally obliged to apply the forceps. The mother had not been well for some days, and Dr. Sears informed me that the amniotic fluid was exceedingly foul.

Three hours after birth the child had a temperature of 99.6°. On the following day her temperature was 100.5° in the morning and 104.4° in the evening. During the first twenty-four hours she vomited a dark brown substance. On the second day, material of the same character was repeatedly vomited. When the patient was thirty hours old, blood and mucus were found in the stools. When I saw the child, she was still vomiting blood and likewise passing blood with the stools. She had had a general convulsion. The skin was not jaundiced, nor were there any petechiæ on the body. Her temperature had been 104.2° at nine in the morning, and at the time of my visit was 102.2°. On the next day the bleeding from the bowels was less pronounced, and the child had a bloody discharge from the vagina. Its intestinal tract had been cleared out with calomel followed by citrate of magnesia, and the large intestine washed out with a normal saline solution. The mother was advised not to nurse the child. By May 29 there was no more blood to be discovered either in the stools or from the vagina. On June 2 the child was again put to its mother's breast on three occasions, and each time it suffered a great deal of distress and vomited sour curdled milk. No further attempt was made to have the mother nurse the child, and from this time forward, with careful regulation of artificial feeding, no further unpleasant manifestations were experienced.

Hemorrhage of the newborn of toxic origin, and in this class we must without doubt place this last case, is usually regarded as a very serious condition. Townsend,[4] of Boston, collected 709 cases in which a mortality of 79 per cent. occurred. That this condition is not of frequent occurrence is evident from the fact that in 5225 births at the Lying-in Hospital in Boston, but 32 instances of this kind are recorded, that is, a little over 0.5 per cent. At the Lying-in Asylum of Prague, in 13,000 births it occurred 190 times, or in about 1.4 per cent. of the newborn. Hemorrhage of the newborn was one of the subjects discussed by the section on diseases of children at the annual meeting of the American Medical Association in 1906. Litzenberg,[5] in that discussion, referred to the case of a babe who thirty-six hours after birth had hemorrhages from the mouth and intestines, the loss of blood being so great that it resulted in death when the child was fifty hours old. At the autopsy innumerable submucous hemorrhages were discovered beginning at the cardiac orifice of the stomach and extending to the rectum, increasing gradually in size from above downward. From these hemorrhagic areas a pure culture of the bacillus of Friedländer was recovered.

One of the most excellent papers on the subject of hemorrhage

[4] Quoted by McClanahan, Jour. Amer. Med. Assoc., October 13, 1906.
[5] Jour Amer. Med. Assoc., October 13, 1906.

of the newborn due to septic or toxic conditions was presented by von Dungen.[6] The literature on this subject is very carefully reviewed by him, beginning with the work of Weber in 1854. Klebs, in 1875, was the first to discover microörganisms in the hemorrhagic areas. He succeeded in producing hemorrhagic peritonitis in a rabbit by inoculating it with the hemorrhagic peritoneal fluid taken from a child who had died of this condition.

Rehn, in 1877, reported the case of a child who died three days after birth from hematemesis and bloody evacuations from the bowels. At autopsy some thirty points varying in size from a pin-point to a pin-head were found in the mucosa of the stomach. Each presented an infiltrated base, in which microörganisms were found. Babes, of Bucharest, was one of the earliest contributors to this field. He discovered specific organisms not only in the hemorrhagic areas, but also in infarcts in the spleen and lungs of a child dying when aged five days, and these he stated resembled the capsulated cocci of pneumonia. V. Dungern concluded that these hemorrhages resulted either from emboli or the damage done to the vessel walls by the production of toxins. In the inoculation of animals the pathological changes he stated are found to be due to the latter. He is rather inclined to believe that the hemorrhagic conditions of early life result from the toxins rather than the bacillary invasion.

Let us consider next the occurrence of gastric or intestinal hemorrhage as the initial manifestation of a toxemia in the adult. Permit us to present 2 cases. In one the hemorrhage was not externally visible, while in the other it was exceedingly profuse.

The first case has been fully reported in the *Medical Record* of February 7, 1903, and, therefore, at this time will only be summarized. It concerned a woman, aged thirty-seven years, who was suddenly seized with acute abdominal pain, at first general, and finally becoming centered in the right side of the abdomen. The only difference between her suffering and that encountered in the ordinary cases of appendicitis was that while the most acute point of pain and tenderness was at the characteristic site of the appendix, there was also severe pain in the region of the gall-bladder and umbilicus. There was marked resistance of the right rectus muscle, which was not altogether limited to the lower half. The temperature was 104.5°, and the pulse rate, 132. One of us (Dr. Jacobson) operated upon her on February 23, 1910. Bleeding was exceedingly profuse. The appendix was found to be 5 inches long, apparently acutely inflamed, at least it was exceedingly red. It contained a mucoid secretion which was not bloody, but in the substance of the appendix there was marked interstitial hemorrhage, which was responsible for the decided enlargement of the

[6] Zentralbl. f. Bakter. u. Parasitenkunde, October 28, 1893.

organ. Nothing unusual occurred in the progress of the case until the fourth day, when the patient developed a hacking cough, and raised a large quantity of bright red blood. During the same night she had a profuse nasal hemorrhage. On the following day petechiæ appeared on the surface of the body, first on the left leg near the head of the fibula, and then numerous ecchymoses showed themselves on the calves of both legs. On the abdomen numerous petechial points were likewise found. The heart at no time presented a murmur nor any other evidence of disease. The joints were not implicated. She never had visible hemorrhage from the intestines or stomach, nor was there hematuria. Nasal hemorrhages were very profuse and frequent, and the bronchial hemorrhage most persistent. The latter continued for nearly three weeks. Whenever she was given a hypodermic injection she bled freely from the puncture of the skin. She made a slow recovery, and has never had any hemorrhagic disturbance since. No member of her family has been a hemophilic. The case was reported as one of purpura, in which the earliest manifestation was hemorrhage into the substance of the appendix.

In reviewing the literature at that time I called attention to a paper published by Professor Henoch.[7] He referred to 4 cases which had come under his observation, all of them occurring in early life. The ages of his patients were four, eleven, twelve and fifteen years respectively. Three of the patients suffered from characteristic joint disturbances which appeared in advance of any gastric or intestinal symptoms. Each of the 4 suffered from pronounced intestinal hemorrhages, but none of them from hemorrhage of any other mucous surface. In each of these cases there were periods of remission and recurrence so that one patient had five attacks in the course of seven weeks, another four in as many weeks, the third had five recurrences and the fourth a similar history. In none, however, was there any evidence of disturbance in the region of the appendix. Each of his patients suffered from marked abdominal tenderness and vomiting, as well as intestinal hemorrhage. The intestinal pain was so severe as to cause loud outcries on the part of his patients, to rob them of sleep, and was associated with marked distention of the abdomen as well as tenesmus. The temperature in all of them was moderate. Each made a good recovery. As, however, his cases were reported in 1874, before the days of bacteriological study, there was no determination of their etiology.

Our last case is of a quite different type. The following history is furnished by one of us (Dr. Post).

M. H., married; aged forty-eight years, inspector of coal, was seen April 8, 1911. He complained of being exceedingly weak and

[7] Berl. klin. Woch., December 21, 1874.

faint. His family and personal history were free from tuberculosis, malignancy, rheumatism, and syphilis. He stated that he had always been well until ten days before. At that time he complained of pain in the lower part of the left side of his chest, which was aggravated by coughing. He consulted his family physician at Newark, N. J., who strapped the chest. The patient in the meantime having been sent to this city to inspect some coal, continued to work until the present illness. On April 6, 1911, in the evening, while at dinner, he became faint. He finished his meal, however, and indeed worked on the following day, but noticed that when he would get up from a squatting position he became dizzy. On April 7 he was about the hotel. He had no desire for food, and during the morning had three or four black tarry stools. That night he was restless, and did not sleep well. When seen on April 8, 1911, he was confined to his bed, was pale, but complained of nothing but weakness. He was anxious to return to his home in Newark, but evidently was not well enough to make a railroad journey of more than three hundred miles. The pallor of his conjunctivæ, lips and mucous membranes suggested that he had sustained a considerable loss of blood. The pulse was 100; temperature normal. Physical examination of the chest was negative. On the left side of his chest and back there were the marks of the adhesive plaster which had been removed. On this date the heart was found to be of normal size. The sounds were faint, but there were no murmurs. The liver and spleen were of normal size. There was no abdominal distention nor tenderness. Rectal examination was negative. April 9 his condition became alarming. The pulse rate was 120; its quality was small and very weak. During the night he had vomited once, the vomitus containing a quantity of fresh blood. The heart sounds had somewhat changed. There was a soft systolic murmur to be heard at the left sternal margin opposite the fourth rib. He was transferred to St. Joseph's Hospital and was there seen in conjunction with Drs. Flaherty and Jacobson. The respirations on admission were 24, pulse, 128; but so weak that it was hardly perceptible. The temperature on admission in the morning was 100.4° per rectum, and at two o'clock in the afternoon it rose to 101.4°, at six o'clock had fallen to 101°, and at ten o'clock to 99.8°. On admission into the hospital he complained of pain in the epigastric region but this disappeared after he was catheterized. He had no abdominal pain nor distress except when the bladder became distended. Each time that he was catheterized at least twenty ounces of urine were withdrawn. On being questioned, he, as well as his wife, stated that he had never had any previous gastric or intestinal disturbance, and that at no time in his life had he suffered from indigestion, abdominal pain, nor anything to suggest a pathological condition in the stomach or abdomen. Physical examination of the abdomen did not reveal

at the time one of us saw him in consultation, any tenderness, rigidity, or dulness. The heart murmur steadily increased, and could be heard loudest on a level with the nipple at the left sternal border. It was least distinct at the base, and was associated with the first sound. On the left side of the chest and corresponding with the area to which the adhesive straps had previously been applied were a number of pigmented spots, which did not fade out on pressure. A blood count was made, and it was found that the hemoglobin was 55 per cent.; red blood cells, 2,250,000; white blood count, 7,000. Dr. F. M. Meader was requested to make a blood culture. His report read: "Specimen consists of about 7 c.c. of blood put into two flasks, each containing about 150 c.c. bouillon. Diagnosis: Pure culture of pneumococcus." His bacteriological diagnosis was based upon the morphological features alone. He made no further cultures upon other media, nor did he make any inoculations. Had he done so, he stated that possibly he might have decided that we were dealing with a capsulated bacillus of the Friedländer group, but not necessarily the pneumococcus.

The patient required catheterization for the first five days after admission into the hospital. The bowel movements continued to be black for four days, evidently containing large quantities of blood. Urinary analysis never revealed any abnormal condition. Blood examinations showed steady improvement. On April 16, the hemoglobin had increased to 60 per cent., the red blood cells to 3,000,000, and the white blood cells numbered 7800. On April 22 the hemoglobin percentage was 65, red blood cells, 3,170,000; and white cells, 5600. At this time he was able to take ordinary foods; had gained in strength, and was able to sit up. The heart murmur had entirely disappeared, and there had been no further evidence of hemorrhage in any form. The temperature continued slightly elevated for a few days. He was discharged from the hospital well on May 8, 1911, and has continued to enjoy excellent health since.

It is evident that in this particular case a capsulated bacillus, probably the pneumococcus, was responsible for the toxemia which produced such a profuse hemorrhage from the intestinal tract. Evidently the site of the disturbance was the duodenum, inasmuch as it was associated with marked gastric hemorrhage. It seems fair to assume in view of the chest manifestations which preceded the intestinal disturbance, that the portal of entry of the infectious organism was pulmonary.

The literature of this class of cases is not abundant. That capsulated bacilli are responsible for gastric or intestinal hemorrhages has been thoroughly established by Howard.[8] After carefully

[8] Jour. Exper. Med., March, 1899.

reviewing the literature and work of others, and as a result of his own studies, he concludes that in the cases of hemorrhagic septicemia there has been found each time a pleomorphic capsulated bacillus. Speaking of the manner in which these capsulated bacilli differ, he says: "Of these differences the chief relate to the various amounts of gas and acid production, the capability and rapidity of the coagulation of milk, the behavior of Gram's stain, and the widely varying results of animal inoculation." He reaches the conclusion that various bacteria, not only those of the group mentioned, but streptococci and others as well, may cause hemorrhagic infection of human beings. Hemorrhagic septicemia is, therefore, not to be regarded as a separate and distinct disease with definite and constant etiology, uniform anatomical lesions and clinical features, but rather as a toxemia attended by such marked injury to the bloodvessels and to the blood as to cause extreme dilatation of the vessels and hemorrhages with various harmful effects upon the body cells. Some of the cases have manifested a rapidly malignant course, while others have been of a milder type and of longer duration.

That the pneumococcus is capable of producing such a hemorrhagic condition has been clearly demonstrated by Claisse.[9] He refers to an unpublished case in the service of Hutinel at the Hopital des Enfants, in which purpura followed upon pneumonia, and in which the pneumococcus was recovered not only in the purpuric areas of the skin, but also in infarcts in the kidneys and spleen, as well as from the endocardium. The character of the microörganism was further established by the inoculation of mice and by cultures. He also demonstrated that the penumococcus can enter the body and produce widespread pathological changes before it awakens a pneumonia.

In this case reported in detail by Claisse he was unable to determine the portal of entry of the pneumococcus. At the time of the admission of the patient into the hospital he was covered with purpuric spots, and was suffering from endocarditis and nephritis. The patient, a young man, aged twenty-two years, had been in good health until, while rendering military service, he had an attack of rheumatism. This became complicated with endocarditis, and thereafter he suffered from dyspnea on the slightest exertion. He had also marked periods of palpitation of the heart, and frequent attacks of bronchitis accompanied by mild hemoptysis. He was poorly nourished, and had become reduced in strength. When admitted into the hospital the petechiæ covered both of his lower extremities, the distribution being symmetrical. There was an increase of splenic dulness and the spleen was large and tender. The precordial region was painful, and there was

[9] Archiv. de med. experimentale et d'anatomie pathologique, 1891, iii, 379.

increased precordial dulness. A mild systolic murmur could be heard radiating toward the armpit. Examination of the lungs was negative. The urine contained a large percentage of albumin. Two days later he was seized with severe pain in the right side of his chest, associated with a prolonged chill. Respirations became labored and frequent. He coughed a little, and expectorated bloody sputum. Then appeared the usual physical signs of pneumonia, involving the base of the right lung, and from this he did not rally. The autopsy justified the conclusion that while the man had had an old endocarditis resulting from the attack of rheumatism, he had in some way become infected with the pneumococcus, and an acute pneumococcic endocarditis resulted. None of the organisms were found in the older lesions of the endocardium. Pneumococci were recovered from the spleen and from the kidneys, as well as from various purpuric macules of the skin. Cultures were made on agar and gelatin, and in bouillon. Animals were also inoculated. In these different ways positive proof of the pneumococcic origin of this case was established.

V. Babes[10] has likewise carefully investigated the subject of the bacteria responsible for hemorrhagic infections in the human being. He also attempted to determine whether a single microorganism is responsible for all types of hemorrhagic infections. He concludes that no single specific organism is responsible therefor. He analyzed in his article the labors of other observers as well as his own, and arranges in columns, for the purpose of comparison, the clinical and laboratory features of the various microörganisms. He studied their behavior upon various culture media, and by the inoculation of animals. He was able to determine that bacteria which cause hemorrhagic septicemia in animals do not conform in all respects with those which produce this disturbance in man. He concludes, however, that all of these bacteria possess the common property of having a specific effect upon the bloodvessels causing molecular destruction either of the vessel walls or hyalin degeneration of the bloodvessels. Some of the results he also concludes are due to changes in the blood, and that the toxic products of bacteria are capable of producing not only the purpuric conditions, but can also cause excessive hemorrhages.

Spencer[11] states that the peculiarity of septicemic or toxic hemorrhage from mucous or serous surfaces is their occurrence without the production of a naked eye breach of the surface.

From the foregoing it is evident that certain microörganisms, particularly those possessing the characteristics of the pneumococcus are capable of provoking severe hemorrhages in various parts of the body, and that gastric and intestinal hemorrhage can be the first evidence of such a toxemia.

[10] Zentralbl. f. Backter. u. Parasitenkunde, 1891, ix, 719.
[11] Brit. Med. Jour., December 24, 1910.

THE DIETETIC AND GENERAL MANAGEMENT OF TYPHOID FEVER IN CHILDREN.[1]

By Charles Gilmore Kerley, M.D.,

PROFESSOR IN PEDIATRICS, NEW YORK POLYCLINIC, MEDICAL SCHOOL AND HOSPITAL; ATTENDING PHYSICIAN, NEW YORK NURSERY AND CHILD'S HOSPITAL; ASSISTANT ATTENDING PHYSICIAN, BABIES' HOSPITAL, NEW YORK.

In the selection of food for children in health we are governed by certain well-recognized principles. For proper growth and right development both physical and mental, the food given must be of adequate nutritional value. This constitutes the science of feeding. It must be prepared so that it may be assimilated by the organism. There must be a variety in form and it must be attractive to the senses of taste and smell, and this is the art of feeding.

In illness we have the same child to deal with and the same factors are in control and must be respected even in greater degree than in health, for then we have not that margin for error which health permits. The child ill requires food of a definite nutritional value in assimilable form. This is the science of feeding in sick children. It requires variety and it is necessary that the food selected be made agreeable to the patient, and this is the art of feeding in sick children.

There is no ready-made diet in any illness in a child, neither is there one ready-made scheme for the artificial feeding of infants ill with digestive derangements. Feeding, then, both in sickness and in health, is an art as well as a science, and in the feeding of sick children the art is of equal importance with science. I find it necessary at the onset of every illness to discontinue milk and so-called solid foods, for the reason that in every illness in a child the capacity for food is lessened, and to what degree it is lessened I make it my business to find out. I give a laxative sufficient to produce a few watery evacuations. As a temporary diet, the child is given flavored gruels and perhaps one of the dried milk foods, until the nature of the illness is determined. In typhoid fever the diagnosis is rarely made under a week of observation.

Following out the above management, when the diagnosis is established, we have an intestine free from distention with gas and undigested milk, and we have consequently a patient less toxic and with a lower temperature than would have been the case had freer feedings been allowed. With the diagnosis of typhoid fever positive, I dictate a list of permissible food articles. We will assume that the patient is five years of age. The diet schedule includes gruels, usually two ounces of the cereal to the pint of

[1] Read before the Section on Diseases of Children at the New York Academy of Medicine, November 9, 1911.

water. Gruels are made palatable and their nutritional value increased by the addition of broths or milk sugar or sherry wine. Cereals very thoroughly cooked such as rice, farina, and cream of wheat are served with butter and cane or malt sugar or with maple syrup and butter. Milk foods are rarely given oftener than once a day. Among those used are matzoom, kumyss, Eiweiss Milch of Finkelstein, and skimmed milk. The latter is always given mixed with a gruel and rarely oftener than once a day. The whites of two, three, or four eggs are given daily with orange juice, or frozen with orange juice and cane sugar and served in the form of a sherbet. Lemonade and weak tea, both with the addition of cane sugar, are given between the regular feedings. Early in the convalescence scraped rare steak, custard, soft boiled egg, and junket are allowed. It is advisable to feed the patient lightly for the first few days, until the organism adjusts itself and adapts itself to its changed condition, when freer feeding may be allowed.

It is entirely wrong to assume that the diet we begin with must be continued throughout the attack. Food will be tolerated during the latter part of an illness which could not be taken during the earlier stages. Feedings are given never oftener than at three-hour intervals or less than four hours, in quantities that we know from observation the child will be able to take care of. One of the reasons for the considerable variety is that children soon "go stale" on any one article of diet; if given persistently, it is refused or taken in small quantities. If it is forced, it is very apt to be vomited; or if retained, the child in all probability will not digest it.

The diet schedule for our typhoid patient, aged five years, would be something as follows:

6 A.M. Eight ounces of gruel with sugar or a small amount of broth added. Zwieback or dried bread and butter.

8 A.M. A drink of weak tea with sugar or the whites of one or two eggs with sugar in orange juice.

10 A.M. Farina, cream of wheat, rice, served with butter and sugar, or maple syrup and butter. Drink of weak tea or kumyss or matzoom, or perhaps a dried milk food, such as malted milk or Nestle's Food.

2 P.M. Eight ounces kumyss, matzoom, or skimmed milk diluted with gruel. Zwieback; dried bread and butter if wanted.

4 P.M. Orange egg sherbet or a drink of lemonade or tea and sugar.

6 P.M. Cereal or gruel with sugar and butter or with broth. If skimmed milk has not been given at two o'clock it may be given with gruel at this time.

10 P.M. Gruel with sugar or broth or with wine.

It will be seen that the caloric requirements, 60 to 70 per kilo for the five-year-old child, may easily be supplied by the above

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It will be seen that the caloric requirements, 60 to 70 per kilo for the five-year-old child, may easily be supplied by the above

arrangements of the feeding, although the diet arranged may not be an ideally balanced one. It would be high in carbohydrates, rather low in fat, and perhaps deficient in protein, particularly during the earlier period of the treatment.

Fat in considerable quantity is poorly digested by young typhoid fever patients. It may be given, however, in small amounts when mixed with other foods. Foods containing protein should not be given in considerable amount until we know something of the course of the disease. Milk, scraped beef, and soft boiled eggs are not well borne in young typhoid patients and a temporary reduction of protein is not felt by them.

Carbohydrates such as the cereals and the different sugars are readily cared for when properly prepared and administered. They supply fuel and no bi-products and do not require immediate elimination from the body. Emaciation is prevented through their action as proteid sparers. Mendel and Rose, in the *Journal of Biological Chemistry*, state they found that the excretion of creatin, induced by starvation, is inhibited in rabbits by feeding a diet of carbohydrates, absolutely free from proteins and fats. When the carbohydrates are given in liberal amounts the creatin entirely disappears from the urine. The creatin eliminated is not reduced by feeding a diet of fat alone or by a diet of fat and protein. Experimental interference with carbohydrate metabolism leads to the elimination of creatin, the presence of the creatin being due to a true tissue or endogenous metabolism.

Why not a milk diet? I have used the milk diet and have seen it used in many cases. Because of an early selection of a medical career, I came in close association with country physicians. It is on the farm and in the country village, where the well and the vault for the sake of convenience are built as close to the dwelling as possible, that we find typhoid fever a frequent visitor. I have watched many of these cases ill with typhoid fed on text-book milk, and I have seen the distended abdomen, the high, protracted temperature, the prolonged and active delirium, and later I filled out the certificate, all but the signature. These patients were given milk in copious amounts at two- and three-hour intervals, and milk constituted the sole food and drink. The milk diet is popular because many physicians have never tried any other means of feeding and it is the easiest way. It is easy for everybody but the patient, and he is not consulted. It is easy for the physician, it is easy for the nurse, it is easy for the household; it is much easier for the doctor to order so many pints of milk a day than it is to write out a diet schedule of right caloric values and explain the preparation of the foods suggested.

The mixed feeding is not employed, further, for the reason that physicians fail to realize that other foods may be taken care of easier than milk, and because of the fear of lay criticism for depart-

ing from an established practice. That many people have recovered from typhoid on the milk diet is not to be questioned. That many have not recovered is equally true. We know that typhoid fever is a disease of small mortality. In spite of former unfavorable impressions as to the milk diet in typhoid I used it early in my medical practice because I had been taught that it was right, and if the patient did not do well it was the fault of the patient, and that the system was the correct one. Another very good reason for using milk was that I have never been taught how to use anything else.

My favorable experience in intestinal diseases with a diet other than milk, together with the teaching of Dr. A. Seiber, of New York, led me to use somewhat similar means of feeding typhoid fever patients.

Mortality statistics do not teach us all that may be learned regarding the disease or a method of treatment. The time element as relates to the duration of the illness and the duration of the convalescence is important. My observation in the milk-fed cases is that the illness is more severe, increasing the danger to life, and that the duration of the illness is longer. Emaciation is much greater and the convalescence is consequently much more protracted than those fed as I have indicated. The case in which the temperature period is cut down to from fourteen to twenty days, with little emaciation and prompt convalescence, should not be put in the same class with the case in which the fever lasts from thirty to fifty days or longer, with a convalescence of three or four months, although both had typhoid fever and both recovered.

It is argued that milk is the ideal diet, and the reason given is that it contains all the nutritional elements required by the organism—fat, proteid, carbohydrate, and mineral salts—which is the truth. It is further claimed that milk may be taken in large quantities and be readily digested, which is not true in sick children. The addition of pepsin, hydrochloric acid, etc., has been of no value. I have learned that in order to have a short case and a mild case, the abdomen must be kept flat. Tympanites is an indication of danger regardless of how it is produced. On the milk diet, tympanites is the rule. On the mixed diet suggested, it is the exception. So long as I can keep the belly flat, I know I have the case reasonably well in hand.

Drugs have been of no service, except to produce an evacuation when there are not two in twenty-four hours and to control the evacuation when there are more than four in twenty-four hours.

Most children will be perfectly comfortable with a temperature of 104° or slightly over. Under such conditions no attempt at reduction is made. In most cases, restlessness and more or less irritability will appear when it goes higher. In such instances

hydrotherapy in the form of the cool pack is used. The child's thorax and abdomen are wrapped in a towel at 95° and then the towel cooled by sprinkling with colder water.

For the conservation of vitality, the nervous manifestations must be controlled sufficiently so that the child gets adequate sleep. The pack with cold to the head will usually relieve the restlessness, irritability and sleeplessness.

The advantages claimed for the method of management, briefly outlined, is a milder course, shorter duration, more prompt convalescence, and usually, absence of complications.

VACCINATION AGAINST TYPHOID IN THE UNITED STATES ARMY.[1]

By A. W. Williams, M.D.,

CAPTAIN MEDICAL CORPS, UNITED STATES ARMY; ATTENDING SURGEON, PHILADELPHIA.

The British Army, on the recommendation of Sir A. E. Wright, then an officer in the British Medical Corps, first used antityphoid vaccination for the purpose of rendering troops immune to typhoid. Major F. F. Russell, of the Medical Corps of the United States Army, after a thorough investigation, made a favorable report to the Surgeon General of the use of this measure of prophylaxis, with its results in both the British and German Armies.

A Board of Medical Officers, consisting of the Surgeon General, Major Russell, and several of our distinguished members of the Medical Reserve Corps, was convened at Washington for the purpose of considering the advisability of its adoption in our Army. As a result, in the early part of 1909, on the recommendation of the Board, the War Department authorized its use in the case of volunteers for inoculation.

On the assembly of Maneuver Division on the Mexican border in the spring of last year, all of the troops, numbering 12,801, were subjected to the typhoid prophylaxis. They remained in camp for four months, from March 10 to July 10. Only 2 cases of typhoid occurred during the entire period of encampment. One case of a very mild type, occurring in a private of the hospital corps, who had not completed his immunization, having taken only two doses. The other case occurred in a civilian teamster who had not been immunized.

[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, November 27, 1911. Published by permission of the Surgeon General.

Our results during this period are being criticized by some, who say we would not have had typhoid in the absence of the prophylactic inoculations. As our principal camps were located at San Antonio and Galveston, the existence of typhoid in these cities at that time refutes this. In the city of San Antonio there occurred during these four months 49 cases, with 19 deaths, and in Galveston 192 cases. The civil population in these cities where our principal camps were located serve as a control, and show what would have happened without typhoid prophylaxis.

In the origin and spread of typhoid fever in our army during the Spanish-American War, investigated by a Board consisting of Reed, Shakespeare, and Vaughn,[2] they reported that in certain regiments of regulars the disease developed in three to five weeks, and that more than 90 per cent. of the volunteer regiments developed the disease within eight weeks of going into camp. Among the whole body of troops there were no less than 20,000 cases between May and September. The Second Division, Seventh Army Corps, assembled at Jacksonville, Florida, with 2,000 less in numbers than the Maneuver Division, for the same length of time, same latitude, with an equally good campsite, and an artesian water supply of absolute purity, had 1,729 cases of typhoid, with 248 deaths. As Colonel Kean remarks,[3] "this division was not conspicuously unfortunate in its typhoid record for that time." It is selected for comparison on account of the close similarity of its conditions of service with those of the Maneuver Division.

This experience at the Mexican border with the Maneuver Division, so remarkable in its results, and so thoroughly convincing as to the value of vaccination against typhoid, resulted in the issuing of an order from the War Department making vaccination against typhoid compulsory in our army. This was the first instance of compulsory vaccination against typhoid as a requirement in an army. Up to October 30, 1911, 81,340 persons had been inoculated with prophylactic furnished from the Army Medical School. From the report of the Surgeon General, 1911, for the calendar years 1909 and 1910, only 11 cases of typhoid occurred among the inoculated, with no deaths, while in the non-inoculated part of the army there occurred 304 cases, with 26 deaths.

A comparison between the inoculated and non-inoculated parts of the army is shown by the fact that in 1910 the mean strength of the army numbered 76,230 American troops. Of this 17,978 had been given the typhoid prophylactic (about one-fourth of the army); only 7 cases occurred among the inoculated, with no

[2] Origin and Spread of Typhoid Fever during the Spanish-American War (1898), Harrington's Hygiene, p. 668

[3] The Sanitary Record of the Maneuver Division, Jour. Amer. Med. Assoc., August 26, 1911.

deaths, whereas in the non-inoculated (three fourths of the army) there occurred 135 cases, with 10 deaths. It is not surprising that vaccination against typhoid falls short of giving immunity in some instances. As pointed out in the Surgeon General's report,[4] there are no doubt persons who cannot be altogether protected against infection, just as vaccination against smallpox will not invariably protect against that disease. But the few mild cases, 11 in all, occurring in the inoculated, without a single death, is strong evidence that the disease was modified by the inoculations, although complete immunity was not obtained in these 11 cases.

Vaccination against typhoid as given in the army is administered hypodermically in three doses. The injections are given in the subcutaneous tissue of the left arm at the level of the insertion of the deltoid. The skin is prepared in the usual manner, by scrubbing with soap and water, followed by alcohol, then the skin is painted with a 5 per cent. tincture of iodine before and after the injection. The hypodermic syringe and needle are rendered sterile by boiling. The first dose contains 500,000,000 killed typhoid bacilli in ½ c.c. of sterile salt solution. The second and third dose, each given at intervals of ten days, contain 1,000,000,000 bacilli in 1 c.c. of salt solution.

The injection is given in the afternoon about four o'clock. This in order that the effects of the reaction will wear off during the night. The immediate effect of the inoculation is a smarting pain lasting only for a minute or two, nothing further is noted until four or five hours afterward, when the man may have a headache and a feeling of malaise, and at the site of inoculation a red and tender area about the size of the palm of the hand.

The headache and other symptoms are rarely sufficient to interfere with sleep, and by next morning all symptoms have usually disappeared. Occasionally soreness is noted in the axillary region, and the lymph nodes may become slightly swollen and tender, but the swelling usually disappears in about twenty-four hours, and is never followed by permanent enlargement or suppuration. In over 100,000 injections in not a single case has a hypodermic abscess occurred. The complete immunity to abscesses is undoubtedly due to the small amount of trikresol (0.4 per cent.) used in preparing the vaccine. As an evidence of how slight the effects of the inoculations were regarded by the men, at my former station no difficulty was experienced by me in obtaining volunteers for inoculation to the extent of 90 per cent. of the command.

It is very interesting to note that persons who have suffered an attack of typhoid usually have the severer reactions. Sir W. B. Leishman expresses the opinion that an exceptional severity of

[4] Report of Surgeon General of the Army, 1911, p. 50.

reaction indicates an unusual degree of susceptibility of the individual. So these are apparently cases of hypersensitiveness to infection. A case illustrating this happened in our service last year. A man who had typhoid in 1899 was inoculated in June 1909, receiving two doses. The first dose produced a moderate reaction, while an exceptionally severe one followed the second. In March, 1910, he had a mild attack of typhoid. The conclusion seems warranted that in this case we have an instance of individual hypersensitiveness to typhoid infection.

A few words as to the preparation of our vaccine, the nature and degree of immunity afforded, and the duration of such an immunity. The vaccine[5] which has been used in the army has all been prepared at the Army Medical School at Washington. It has been prepared from a single strain of the bacillus which has been for many years under cultivation, and has practically lost its virulence for animals. It grows luxuriously on agar, and presents the usual characteristics on all laboratory media. Before making a batch the culture is plated out and half a dozen typical colonies are selected for further use. The growth on each of six tubes is washed off in 2 c.c. of broth, and used in the next step, which is the inoculation of a number of Kolle flasks. The cultures are incubated for eighteen hours, each flask carefully scrutinized for contamination, and the growth washed off in salt solution. The emulsion is collected in two liter flasks. The flasks are sunk in a water bath, and kept at 55° C. for one hour after the temperature of bath is reached.

While the flasks are in the bath the emulsion is standardized by counting the bacteria in a sample of the unkilled emulsion. The method is a modification of the one devised by Sir A. E. Wright. Equal parts of the normal human blood and emulsion to be counted are thoroughly mixed. Small drops of the mixture spread on slides are stained, and counts of both the red cells and the bacteria made in a large number of different microscopic fields. Since we know that normal human blood contains 5,000,000 red blood corpuscles per cubic millimeter, it is easy to count the actual number of bacteria from the ratio between the two.

On account of lysis occurring in some of the more delicate bacteria, Major Harrison, of the R. A. M. C., modified Wright's method by washing the red blood corpuscles free from their serum in sodium citrate before adding them to the bacteria. The ratio of bacteria to the red blood corpuscles is not disturbed by the washing of the latter, since they are equal in the beginning. The counts obtained from the broth cultures of the bacillus after forty-

[5] Russell, New York State Journal, December, 1910 (this report has been drawn on very freely by the author, particularly laboratory technique, etc., as regards preparation of prophylactic).

eight hours' incubation run from 1,200,000,000 to 1,400,000,000 bacteria to the cubic centimeter, hence the stock culture must be diluted with salt solution until 1 c.c. contains approximately 1,000,000,000 bacteria. To the standard emulsion is added 0.25 per cent. trikresol, thus making it doubly certain that all the bacteria are killed. It is put up in sealed glass ampules. Each container is labelled with the name and number of the product, and given a date three months from the time of its preparation, after which it should not be used.

Investigations of blood changes following vaccination against typhoid were made by Pfeifer and Kolle in 1896. They showed, from a thorough and exhaustive study of the specific changes in the blood serum, that not only were agglutinins produced, but what is more important, that the bacteriolytic power of the blood was also raised in the same way as during an attack of typhoid. So far as is known at present we have, then, the same antibodies produced as a result of inoculation as are produced during clinical typhoid, and the quantity of agglutinins, bacteriolysins, and opsonins seems to be even greater after vaccination than after clinical typhoid, and it is therefore not unreasonable to expect that the immunity conferred by vaccination will last for a considerable period. From tests made at the laboratory of the Army Medical School of a large number of vaccinated persons, the Widal was invariably positive after vaccination, in many cases being present in dilutions of 1 in 5,000, 10,000, or even 1 in 20,000, and usually remaining present for nearly a year, in some instances for seventeen and twenty months.

As to the length of time immunity is offered after vaccination, this cannot be definitely answered at present, and until observation can be made over a prolonged period this question cannot be accurately determined. The present plan in the Army is to vaccinate every three years.

As modern wars are unlikely to last over three years, what an ideal agent we have for the control of the most dreaded camp disease. A disease which, during the short life of the Spanish-American war, claimed 20,738 victims, with 1,580 deaths, or 86.24 per cent. of the entire mortality of the war. The application of this prophylactic, so ideal for the army, is no less important to the nurse in training, the hospital attendant, the interne, the physician, and in the face of an epidemic, the community.

AN EXPERIMENTAL STUDY OF HIGH INTESTINAL OBSTRUCTION.

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Intestinal obstruction in man, if unrelieved, speedily causes death. The fatal outcome is too rapid to be the result of starvation, and three general theories have been advanced to explain it: (1) A disorder of the nervous mechanism controlling the cardiac and vasomotor systems. (2) A bacterial infection of the organism by the passage outward of bacteria from the intestinal lumen. (3) An intoxication from poisonous substances imprisoned in the intestine orally to the obstruction.

The advocates of these various theories have done a vast amount of experimentation to uphold one or the other, but up to the present time the question remains unsettled.

The Theory of a Nervous Disorder. In favor of the first theory, clinical evidence has been adduced. The tachycardia, the low blood pressure, the profound collapse of the patient, and the wide dilatation of the splanchnic bloodvessels all point to a loss of activity on the part of the medullary nerve centres. The early writers saw in these the result of a reflex disturbance from stimuli acting on the nerve endings in the intestinal wall. It is undoubtedly true, however, that exactly this train of events may arise from a toxemia or a bacteremia without the intervention of any afferent nerve impulses.

Recently, Braun and Boruttau,[1] have modified this theory somewhat, and assign the above symptoms to a disturbance of the circulation resulting from interference, chiefly mechanical, with the inherent nerve plexuses in the intestinal wall. They see a parallel between a gradual bleeding to death and the death in intestinal obstruction. The loss of body fluids resulting from failure of absorption, the enormous outflow of fluid into the intestine, the persistent vomiting, and the stagnation of blood in the splanchnic area lead to an anemia of the brain centres which progresses till these centres cease their activity, and death results. They experi-

[1] Deutsch. Zeitsch. f. Chir., 1908, xcvi, S. 544.

mented most exhaustively on rabbits to support this view, but the evidence is all indirect, and seems to us not to amount to a proof of the absence of a toxemia. We are unable to find in the literature any experimental work which is convincing that the nervous system is primarily at fault. Certainly, as death approaches, there is a profound disturbance of the nervous control of the heart, bloodvessels, and respiration, but this, we believe, is in no sense a reflex disturbance, nor the result of an anemia, *per se*, of the nerve centres.

The Theory of Bacterial Infection. The infection theory has much more to substantiate it. The intestinal lumen is the normal habitat of innumerable microörganisms which are potentially pathogenic. When an obstruction exists, these no longer have their normal outlet *per anum*. They are dammed up in the intestine under favorable conditions for their growth (McClure[2]). The damage to the intestinal mucosa may allow their passage outward, either into the blood stream, the lymphatics, or directly into the peritoneal cavity. Proof of this possibility is seen clinically in the presence of a peritonitis as a complication of intestinal obstruction without perforation; also in the frequent finding of the colon bacillus in the blood as a pathogenic microörganism, under very varied conditions of intestinal disturbances less severe than an obstruction, and in the bacteremia from the Bacillus typhosus when the intestine is ulcerated by the action of that organism.

Von Khantz,[3] experimenting on rabbits in a low intestinal obstruction, often found a bacterial invasion of the blood and the peritoneum, but never the former without the latter. Borszesky and von Genersich,[4] on the other hand, found a blood infection with no invasion of the peritoneum. There can be no doubt that a bacterial invasion of both the peritoneum and the blood may take place in intestinal obstruction, but it is not an essential accompaniment. It occurs late as a complication, often a terminal one. Both clinically and experimentally it will result most often when the obstruction is complicated by a strangulation. Without this complication, intestinal obstruction will kill with no passage of bacteria beyond their normal place of occurrence in the bowel lumen.

The tables on pages 362 to 363 give the result of our experiments bearing on this point. In the first series the obstruction was produced by dividing the intestine from 10 to 30 cm. below the pylorus, and closing the ends by inversion. It will be noted that in all these cases some microörganisms were found in the organs examined.

[2] Jour. Amer. Med. Assoc., 1907, xlix, 1003.
[3] Arch. f. klin. Chir., 1909, xxxviii, p. 412.
[4] Beiträge z. klin. Chir., Band xxxvi, S. 448.

This, we believe, was due to two factors, namely, the necessary local soiling of the peritoneum by the method of operating, and the fact that all the examinations were made several hours post mortem, because the animals died during the night. In the second series, however, the obstruction was produced by the clamp described below, and the animals were either killed when it was believed they were too sick to live over night, and immediately examined, or the examination was made very soon after the animal died from the obstruction itself. This series of 7 cases furnishes irrefutable proof that death results from an obstruction of the upper intestine in the dog, without any invasion of the peritoneum, blood, liver, or spleen by bacteria, which are demonstrable by the methods employed. The methods in the two series were exactly similar and their efficiency in detecting organisms is amply demonstrated in the first. The cultures were taken at autopsy on slant agar or Loeffler blood serum or both. Usually four tubes, sometimes only three of each were inoculated from each tissue, and grown under both aërobic and anaërobic conditions at incubator temperature. For the anaërobes the Buchner method or the Cornell modification of it was used. The tubes were examined at the end of one, two, and three days. All the cultures were made in the sterile room of the Cornell bacteriology laboratory. This consists of a closed cabinet, ventilated through a bacterial proof filter, in the roof of which is suspended an ordinary revolving lawn sprinkler. The water is turned through this for fifteen or twenty minutes prior to taking the cultures. Thus the air is mechanically sterilized by washing out the microörganisms. All the needed apparatus for taking the cultures and smears is assembled before beginning the inoculations, and the air-tight door is kept closed until all cultures are completed. The technique in making the inoculations is that usually employed in obtaining cultures from postmortem material. The efficiency of the room and the method is demonstrated by the fact that only three air contaminations were found in several hundred tubes.

In some of the later cases of the second series no cultures were taken from the spleen, since it was noted that this organ never showed infection when the liver and peritoneum were without infection. Often, too, the spleen cultures gave no growth when the other organs were actively infected. A summary of this series shows that the femoral blood was cultured seven times and always was without growth; the liver was cultured six times, and showed one colony of Gram-positive cocci, in one tube of one case, probably an air contamination; the results from the peritoneal cultures were exactly the same as from the liver; the spleen was cultured only twice, with negative findings both times; the jejunal or duodenal contents above the clamp were cultured seven times, and all tubes showed an abundant growth of various microörganisms.

SERIES 1

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
12	Spleen	2 aërobic 3 anaërobic	None	1 aërobic 2 anaërobic	Morphology and growth characteristic of colon bacillus on usual differential media	Intestine sectioned and closed 34 cm. distal to pylorus. Lived eighty hours. Cultures taken ten hours postmortem.
	Liver	2 aërobic 4 anaërobic	All	All	(1) Gram + coccus. (2) Bacillus identified as colon on differential media. (3) Also very many colonies of a large gram + anaërobic bacillus with morphology of bacillus aërogenes capsulatus.	
	Jejunum	2 aërobic 4 anaërobic	All	All	(1) Gram + coccus. (2) Large anaërobic Gram + bacillus. (3) Gram − bacillus of two kinds, first long and slender; second, short and plump. Both grew in anaërobic tubes, while the former only grew in aërobic tubes.	
13	Femoral blood	4 aërobic 4 anaërobic	None	None		Intestine sectioned 36 cm. from pylorus and ends closed. Autopsy about thirteen hours postmortem.
	Peritoneum	4 anaërobic 4 aërobic	4 aërobic 4 anaërobic	None	(1) Gram + and (2) Gram − coccus.	
	Spleen	4 aërobic 3 anaërobic	1 aërobic	None	Gram + coccus. Same organism as in peritoneum.	
	Liver	4 each	None	None		
	Jejunum	4 each	All	All	Same as in Case 12.	Cultures taken from jejunum when it was sectioned at operation gave the same results as at autopsy.
14	Jejunum at operation	2 aërobic 2 anaërobic	All	All	(1) Gram negative bacillus. (2) Gram + coccus. (3) Large Gram + bacillus	Intestine sutured after section 31 cm. from pylorus. Autopsy thirty-six hours postmortem.
	Jejunum at autopsy	4 each	All	All	(1) Anaërobic gas forming Gram − bacillus. (2) Gram + bacillus. (3) Gram + coccus.	
	Femoral blood	4 each	2 aërobic	All	(1) Gram positive coccus, ferments lactose, and glucose, without gas, no change in neutral red and saffranin. (2) Large anaërobic Gram + bacillus with morphology of aërogenes capsulatus bacillus.	
	Peritoneum	2 each	All	All	(1) Gram + coccus, same as in femoral blood. (2) Gram − bacillus-like colon. bacillus.	
	Spleen	4 anaërobic 4 aërobic	2 aërobic	2 anaërobic	(1) Gram — coccus. (2) Gram — bacillus having the characteristics of coli communis.	
	Liver	2 anaërobic 4 aërobic	2 anaërobic 3 aërobic	None	(1) Gram + coccus as in peritoneum and femoral blood.	

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
15	Jejunum at operation	4 each	4 anaërobic	4 anaërobic 2 aërobic	Gram — bacillus, mobile same as in peritoneum.	Intestine ligated with tape 35 cm. from pylorus. Autopsy four hours post mortem. General peritonitis present.
	Jejunum at autopsy	4 each	1 anaërobic	4 anaërobic 4 aërobic		
	Peritoneum	4 each	4 anaërobic	4 anaërobic 4 aërobic	(1) Gram — bacillus having characteristics of colon bacillus (2) Gram—bacillus intermediate in colon group, changes neutral red and saffranin, does not ferment lactose. (3) Gram + coccus.	
	Femoral blood	4 each	None	None		
	Spleen	4 each	None	None		
	Liver	4 each	None	None		
16	Jejunum at operation	4 aërobic 4 anaërobic		4 anaërobic 4 aërobic	Not identified	Bowel sectioned and inverted 48 cm. from pylorus. Lived about thirty-two hours. Autopsy twelve hours post mortem. No peritonitis.
	Jejunum at autopsy	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	(1) Short Gram — bacillus. (2) Gram + coccus resembling streptococcus. (3) Large Gram + bacillus.	
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Spleen	4 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	Gram — short, stout, bacillus mobile (2 strains), resembling colon bacillus. (2) Gram + bacillus. (3) Gram + coccus.	
	Peritoneum	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	(1) Gram + coccus. (2) Gram + bacillus. (3) Gram — bacillus, short and stout, mobile. Same as in liver.	
17	Jejunum at autopsy	None taken	None taken	.....	.....	Jejunum clamped 37 cm. from pylorus with Crile clamp, which at autopsy was found to have cut through. Autopsy eight hours post mortem, lived about eighty-eight hours. General peritonitis present.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Spleen	4 aërobic 4 anaërobic	1 anaërobic	None	Gram + coccus. One colony outside line of inoculation. Probable air contamination.	
	Liver	4 aërobic 4 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	4 anaërobic 3 aërobic	4 anaërobic 3 aërobic	(1) Gram — bacillus, having characteristics of coli communis. (2) Gram + coccus. (3) Gram + bacillus short and fat and growing in long chains.	

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
18	Jejunum	None taken	.....	.....	.....	Jejunum clamped with Crile clamp 20cm. from pylorus. Killed with chloroform ninty-one hours after operation. Clamp cut through, local peritonitis resulting.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	4 anaërobic 4 aërobic	(1) Gram − bacillus. (2) Gram + bacillus.	

SERIES II.

19	Jejunum	3 aërobic 3 anaërobic	3 anaërobic	3 anaërobic 3 aërobic	(1) Gram − bacillus. (2) Gram + coccus.	Intestine occluded with special clamp 18 cm. from pylorus. Lived one hundred and seventy-two hours after operation. Killed with chloroform. Autopsy immediately. No peritonitis; local abscess around clamp.
	Femoral blood	4 aërobic 3 anaërobic	None	None		
	Spleen	4 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 3 anaërobic	None	None		
	Peritoneum	3 anaërobic 4 aërobic	None	None		
	Abscess around clamp	2 aërobic 2 anaërobic	.....	1 anaërobic 2 aërobic	Gram negative bacilli.	
20	Jejunum	None taken	.....	.....	.....	Occlusion clamp 16 cm. from pylorus. Lived ninety hours. Died. Autopsy. No peritonitis.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Liver	4 anaërobic 4 aërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	None		
	Exudate around clamp	3 aërobic 3 anaërobic	None	None		
21	Jejunum	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	(1) Gram + coccus. (2) Gram + bacillus. (3) Gram − bacillus.	Occlusion clamp on jejunum 16 cm. from pylorus. Dog lived 58 hours. Autopsy 8 hours post mortem. Peritoneum clean.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Spleen	4 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 4 anaërobic	None	None		
	Peritoneum	3 aërobic 4 anaërobic	1 aërobic	.....	Gram + coccus. One colony only, probably air contamination.	
22	Jejunum	3 aërobic 3 anaërobic	2 aërobic 1 anaërobic	.....	Gram + cocci	Occlusion clamp 12 cm. from pylorus. Lived twenty-one days. Killed with ether. Clamp not absolutely tight. No peritonitis.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Liver	3 aërobic 3 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	None		

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristic.	Remarks.
23	Jejunum	None taken	.....	.....	.....	Occlusion clamp 12 cm. from pylorus. Lived two hundred and forty hours. Killed with cyanide and autopsied immediately. No peritonitis. Clamp tight.
	Femoral blood	3 aërobic 3 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	None		
24	Jejunum	2 aërobic 2 anaërobic	.....	2 aërobic 2 anaërobic	Gram positive and negative bacilli	Occlusion clamp 16 cm. from pylorus. Lived two hundred and five hours. Autopsied two hours post mortem. No peritonitis. Small abscess around clamp which was tight.
	Femoral blood	3 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 4 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	None		
	Clamp Abscess	2 aërobic 2 anaërobic	2 anaërobic 2 aërobic	.....	Pure growth of Gram + coccus.	
26	Jejunum	4 aërobic 4 anaërobic	..... None	4 aërobic 4 anaërobic	(1) Small Gram negative bacillus. (2) Large, long Gram + bacillus	Occlusion clamp 16 cm. from pylorus. Lived two hundred and forty hours. Killed with ether. Autopsy immediate. No peritonitis.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Liver	3 aërobic 4 anaërobic	1 aërobic	None	One colony outside inoculation of a Gram positive coccus.	
	Peritoneum	4 aërobic 4 anaërobic	None	None		
28	Jejunum	2 aërobic 2 anaërobic	2 anaërobic	2 aërobic 2 anaërobic	Gram positive and negative bacilli and negative cocci. Anaërobic tubes show gas production.	Occlusion clamp 11 cm. from pylorus. Lived fifty-six hours. Autopsy ten hours post mortem. Abscess around clamp. No peritonitis. Clamp tight.
	Femoral blood	4 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 3 anaërobic	None	None		
	Peritoneum	4 aërobic 4 anaërobic	None	None		
	Clamp abscess	2 aërobic 2 anaërobic	None	None		

Case 22, is not included in the above summary because the obstruction was not complete. It is worthy of note here, however, that the jejunal tube only showed a growth of a Gram-positive coccus in one-half the tubes inoculated, showing that the long period (twenty-one days) with only sterile water by mouth did much toward sterilizing the upper bowel.

THE INTOXICATION THEORY. This theory has experimental evidence to support it, and no experiments have proved the absence of a toxemia. Clairmont and Ranzi[5] demonstrated that the stagnated material above an obstruction, after passage through a Reichel or Pukal filter, was exceedingly toxic when injected into the blood of an animal. Kukula[6] found a toxic material in the alcoholic extracts of the intestinal contents in experimental ileus. Roger,[7] and Roger and Garnier[8] went farther and proved that the normal content of both the stomach and the intestine are poisonous when thus injected. They did not filter it, but death occurred too early to be the result of an infection. The toxicity was only one-third as great when injected into the portal vein as when injected into a peripheral vein. They also injected it into a mesenteric artery, against the current, so that it was carried backward and then redistributed through branches to a considerable section of the intestine. Here it produced emboli and stopped the absorption, so that large doses were not fatal. This power to cause clotting in the vessels of the intestine is mentioned in this connection because it may account for the gangrene resulting in some of our experiments (see page 386). Murphy and Vincent[9] found the material from the obstructed or strangulated intestine very poisonous when injected into the peritoneal cavity, and that its poisonous properties were destroyed by boiling or passage through a Berkefeld filter. They concluded, therefore, that living bacteria are the important factors. It does not seem to us that this conclusion is tenable. Their experiments only prove that living bacteria, if they obtain entrance into the peritoneum, will kill. They do not disprove the presence of other poisons in the obstructed intestine, which, being slowly absorbed over a period of some hours, or days, will kill with the symptoms of ileus. Such poisons may be constantly elaborated and absorbed, but may never be present at any one time in sufficient quantity to cause death when injected into the peritoneal cavity. The symptoms arising from the injection of the intestinal contents into the blood, as reported, differ very markedly from those appearing in the obstructed animal, and there are many objections as pointed out by Guibe,[10] Braun and Boruttau,[11] Korentchevsky,[12] and others, against accepting these experiments as directly bearing on the cause of death in intestinal obstruction. The lessened absorption from the obstructed intestine is one objection offered. Clairmont and

[5] Archiv f. klin. Chir., 1904, Band lxxiii, S. 696.
[6] Ibid., Band lxiii, S. 773.
[7] La Revue Scientifique, January 19, 1907, vol. i; La Presse Médicale, January 4, 1911.
[8] Archiv. de med. Experiment, July, 1906; Revue de Medicine, August 10, 1906; La Presse Médicale, May 23, 1906.
[9] Boston Med. and Surg. Jour., November 2, 1911.
[10] La Presse Médicale, April 3, 1909.
[11] Loc. cit.
[12] Roussky Vratsch, 1908, p. 1572. (Cited by Guibe.)

Ranzi[13] found that potassium iodide placed in the bowel above the obstruction, was excreted from the kidneys in greater quantities than normal, up to eight or ten hours after the obstruction was produced, the excretion rapidly decreased after that, and came to a stop in about fifteen hours. Braun and Boruttau[14] gave strychnine to their obstructed animals, and from the resulting symptoms they concluded that absorption became markedly reduced from the start. On this experiment they base their chief objection to the intoxication theory. However, as we shall show in our experiments, the development of symptoms is very slow, and death, under proper precautions to exclude damage to the intestinal wall, may be long postponed, so that a minimal absorption of poison is all that is required. A more important objection, than the lessened absorption, to using the evidence of the injection experiments as a proof of the intoxication theory, is that many substances injected directly into the circulation are poisonous, whereas, if they have to pass through living cells to get into the blood, their poisonous properties are entirely destroyed. Peptone is such a substance, and is a good illustration in this connection. The injection of peptone into the blood produces symptoms of poisoning, which may end in death. The absorption of peptone from the intestine is, on the contrary, a normal physiological process. Therefore, the mere presence of substances in the obstructed intestinal tract, which act as poisons when injected into the blood, is no indication that these substances cause the death resulting from an obstruction, since they are normally found in the intestine in conditions of continued health. To accept the view that such a death results from a toxemia it must be conceived either that new poisons are elaborated and absorbed or that an abnormal absorption of the poisons normally present takes place. In undertaking our work, after a study of the literature, we tentatively accepted the first hypothesis and planned our experiments to determine by a process of exclusion from what sources such new poison or poisons arise. In this endeavor we were only partially successful, but as the work developed the second conception was forced upon us, namely, that the essential factor in causing the symptoms and death in intestinal obstruction does not lie in the poisons *per se*, but in the production of lesions which favor their abnormal absorption. We believe our readers will get a clearer understanding of our findings if he will follow, step by step, the reasoning and experiments which led to this change of conception in our minds.

In searching for the source of the poison we accepted three possibilities: (1) Foodstuffs or substances derived from them; (2) true bacterial toxins; (3) secretory substances from the ali-

[13] Loc. cit. [14] Loc. cit.

mentary tract and digestive glands, or their derivatives. It was our intention to exclude one after the other of these possible sources and study the conditions resulting after an obstruction was produced. It is readily conceivable that there may enter into all of these the result of bacterial activity. While, as detailed above, our experiments have shown that a bacteremia is not necessarily present, they have not excluded either a bacterial toxin or substances developed by virtue of the presence of bacteria in the occluded bowel. Indirectly, however, there is some clinical and experimental evidence that bacteria are not an essential in the process. Clinically, we know that a high obstruction produces much more severe symptoms, and is more rapidly fatal, than a low obstruction. The bacteria, however, are much more numerous in the lower bowel than in the upper. Roger and Garnier[15] found the most toxic substance in the duodenum; the least in the colon. The toxicity, too, was greater in unobstructed conditions, than in the obstructed conditions, and it grew less the longer the obstruction continued, while McClure[16] has shown that the bacteria increase rapidly when an obstruction is produced. Vidal[17] found that the toxicity could be decreased by injecting, simultaneously with the duodenal contents, glycerin extract from the jejunal mucosa lower down, and this cannot be explained on the ground that bacteria are the exciting cause of the poison. V. Baracz[18] found that dogs with a double occlusion of the lower ileum and cecum might live for many weeks. At the end of this time only a moderate quantity of material was found in the loop. The contents were rich in bacteria. The intestinal wall showed marked changes; mostly in the form of an hypertrophy, but sometimes an atrophy was present. The microscopic findings are not given. In one case the animal was killed after four hundred and twenty-five days while in a condition of perfect health. Here the bowel loop, about 20 cm. in length, was found enormously distended, filled with 365 grams of a foul-smelling, greenish material, which was rich in bacteria; a bacillus, the Bacterium aërogenes and a leptothrix being isolated in cultures. These cases seem to point to the conclusion that the stagnation of bacteria and their toxins in the intestine is not sufficient to cause the symptoms seen in intestinal obstruction. Indeed, they, with the facts cited immediately above, seem to make it doubtful whether microörganisms play any essential part, either directly or indirectly, in producing these symptoms. This question, however, must remain an open one for the present, and the writers can offer no positive answer to it.

There still remain the stagnated foodstuffs, and the stagnated glandular secretions of the stomach, intestine, liver, and pancreas

[15] Loc. cit.
[16] Loc. cit.
[17] Revue de Chir., October 10, 1900, xxii; Congres. Francais de Chir., 1905, xxviii, 1237.
[18] Archiv f. klin. Chir., Band lviii.

as the source of the poisonous materials. Draper,[19] of Rochester—formerly Maury of New York—has worked on the theory that the duodenum secretes a substance or substances which normally are rendered non-toxic by passing over the jejunal mucous membrane lower down. When obstruction is present the duodenal substances are not brought into contact with the antibodies, and, hence, remain poisonous and cause death. Vidal earlier advanced this view.

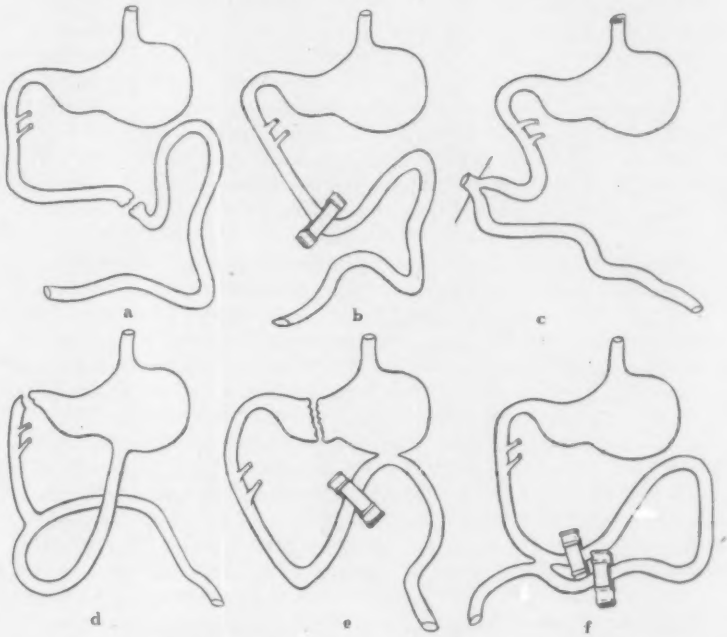

FIG. 1.—Showing the types of operation done: *a*, obstruction by sectioning and inverting the cut ends; *b*, obstruction by means of the special clamp; *c*, attempt to produce sterile condition of gut by fistula and washing; *d*, elimination of duodenal contents from upper bowel; *e*, double occlusion of one-half of the stomach and the duodenum with reëstablishment of the alimentary canal; *f*, the same in the small intestine distal to the duodenum.

Draper has done some elaborate experiments in the way of side-tracking the various secretions to support this theory, but his reports are somewhat contradictory, and he himself says very inconclusive. Recently he has reported that feeding dogs which have an obstruction just distal to the duodenum, with the excised mucous membrane from the jejunum and ileum of other dogs,

[19] Jour. Amer. Med. Assoc., October 21, 1911; Johns Hopkins Hosp. Bull., 1909, p. 838; AMER. JOUR. MED. SCI., vol. cxxxvii, p. 725, and Jour. Amer. Med. Assoc., 1910, liv, 5.

prolongs the life of the obstructed dogs. The difference between the control dogs and the fed dogs, however, was not marked, and the exceptions where a fed dog died in a shorter time, or one not fed lived a longer time, were too numerous to make the total result at all convincing.

The possible relation of the stagnated foodstuffs to the production of the poisons was studied in the following experiments. The type of operation is shown in Fig. 1.

EXPERIMENTS.

All animals were fully etherized before operation. No food was given in any case after the operation, unless so stated. Water, however, was given freely, unless otherwise noted.

No. 3. A cat which had received no food for ninety-six hours before operation. Duodenum sectioned and ends closed by inversion 10 cm. below pylorus. For three days the animal remained in good condition. Vomited. Fourth day showed marked weakness and some rigidity of muscles of extremities. Just before death had convulsions involving extremities. Killed with chloroform ninety-six hours after obstruction. Autopsy immediate. No peritonitis. Closure of bowel ends tight. Stomach contained small amount of normal appearing gastric content. Duodenum empty. Neither stomach or duodenum was distended.

No. 4. Fox terrier. Fed twenty hours before operation. Repetition of No. 3, the section being 11 cm. distal to the pylorus. Except for some weakness and vomiting, seemed like normal dog for four days. Died with progressive weakness and vomiting on seventh day. Autopsy. No intestinal leakage. No peritonitis. Stomach slightly distended. Duodenum not distended.

No. 5. Bitch. Weight 9.8 kgr. Fed last time forty-eight hours before operation. Repetition of No. 3. Post-operative course the same. Lived one hundred hours. Autopsy. No intestinal leakage. No peritonitis. No distention of stomach or duodenum.

No. 6. Bitch. Weight 10.85 kgr. Starved for seventy-two hours. Repetition of No. 3, section being 12 cm. below pylorus. Post-operative course the same. Temperature varied from 36.6° to 39° C. Lived for fifty-five hours. Autopsy. Same findings as those given above.

No. 7. Dog. Weight 19.7 kgr. Fed last time forty-eight hours before operation. Same operation 16 cm. below pylorus. Some peritoneal soiling with intestinal contents. Post-operative course same as others, except more acute. Temperature as high as 39.9° C. Lived only thirty-six hours. Autopsy yielded same findings as others.

No. 8. Dog. Medium weight. Fed six hours before operation. Same operation 12 cm. below pylorus. Post-operative course the same. Temperature 39°. Lived one hundred and eighteen hours. Autopsy. Same findings and in addition there were noted three superficial areas in the duodenum which resembled ulcers.

No. 9. Leakage of intestinal contents at closed end of proximal gut.

No. 10. Same.

No. 11. Dog. Weight 5.3 kgr. Fed twenty-six hours before operation. Same operation 33 cm. below pylorus. Lived only ten to fourteen hours. Autopsy. No leakage. No peritonitis. Stomach was not distended. Mucosa showed small punctate hemorrhages. Intestine proximal to section and for 80 cm. distal to it was much congested and showed hemorrhagic areas in it. We are unable to explain these last postmortem findings as being the result of the operation. Our belief, however, is that the early death resulted because of them.

No. 12. Bitch. Weight 9.2 kgr. Fed twenty-six hours before operation. Same operation 36 cm. below pylorus. Post-operative course as above. Lived eighty-two hours. Autopsy. Same findings as in other cases.

No. 13. Dog. Weight 8.2 kgr. Fed twenty-six hours before operation. Bowel sectioned 36 cm. below pylorus and ends inverted. Symptoms same as others. Temperature 35.5° C. Pulse 180 after twenty-four hours. Lived thirty-eight hours. Autopsy. No peritonitis. Ends of bowel tight. At distal closure an intussusception 14 cm. long had taken place and the intestinal wall was much damaged. This, we believe, contributed to early death.

No. 14. Young dog. Weight 5.75 kgr. Fed seven hours before operation. Bowel sectioned and ends inverted 31 cm. below pylorus. Never fully recovered from operation and died in twelve hours. Autopsy. No peritonitis. Closed ends tight.

No. 15. Dog. Weight 10.5 kgr. Fed forty-eight hours before operation. Bowel sectioned and ends closed 48 cm. below pylorus. Post-operative symptoms same as in other dogs. Lived thirty-two hours. Autopsy. No peritonitis. Closed ends tight; 10 cm. intussusception of distal end in gut, with much damage of gut wall. Proximal intestinal mucosa showed much congestion and many punctate hemorrhages.

These animals were operated upon at varying periods after eating, and none was fed anything after operation. The one which lived the longest, one hundred and sixty hours, was fed twenty hours before operation, and the one that died in ten hours was fed the last time twenty-seven hours before operation. One dog which ate a full meal only six hours before operation lived one hundred and sixteen hours, while one that had fasted for seventy-two hours lived fifty-five hours after operation. The dogs had

all the water, both before and after the operation, that they would take.

This same lack of correspondence between the state of digestion at the time the obstruction was produced on the one hand, and the severity of the symptoms and length of life afterward, was noted in all subsequent experiments. It seems, therefore, reasonably certain that decomposition of food residues in the tract has little to do with causing death, although the ingestion of food after the obstruction might readily be a factor.

The condition of the dogs after operation can be very briefly summarized. They showed a remarkable absence of active symptoms. Recovery from operation was usually prompt and complete, and on the next day they seemed well, but less lively than before. There was a slight rise in temperature. Water was drunk freely, and promptly vomited, washing out bile and mucus. Emaciation was marked. After a varying time the animal began to grow weak, but there was a lack of many of the symptoms we are accustomed to see in the human subject. Vomiting, as a rule, took place only after drinking. There was no abdominal distention, and no sign that cramps or colic were present. Once or twice we noted some rigidity of the muscles of the hind legs, as described by Maury, but in most cases no such rigidity could be demonstrated.

An autopsy was done in every case, and in none was there any gross alteration in the organs that accounted for death. The peritoneum was not inflamed. The stomach and the intestine above the section were never markedly distended. They usually contained only a very small amount of bile and mucus. The mucosa showed a severe congestion. In one or two cases there was a superficial ulceration in the intestinal mucosa. We were struck with the fact that the most severe changes of this character were present in the dogs living the shortest time. The gall-bladder was not distended. The kidneys and liver showed congestion, and the former evidence of degeneration.

From these cases it was determined that animals with a high obstruction might live as long as five to seven days; that the length of life was not dependent on the presence of food residue in the tract above the obstruction, and that autopsy gave no gross evidence of the cause of death. A complete microscopic study of these cases was not made. Where sections were examined, however, the same lesions were found in the intestinal mucosa, the kidney and the liver, as those to be described in the second group of cases.

We next turned our attention to the production of an obstruction which should not be complicated by any operative damage to the intestinal wall. This was considered advisable because there seemed to be a direct relation between the severity of this damage on the one hand, and the severity of the symptoms and

the early death of the dogs on the other (Nos. 11, 13, 15). In one case the bowel was closed by tying a tape around it and burying this with a row of Lembert sutures. The tape cut through and a perforative peritonitis followed. The same thing resulted in two cases where the Crile carotid clamp was used.

A special clamp was then devised which proved to be efficient in causing a complete obstruction, without opening the gut, or damaging the blood supply. The clamp consisted of two rubber-covered aluminum plates, about 1 cm. in width and 4 cm. long. Over each end a second covering of rubber tubing was placed. One plate was then passed through a slit in the mesentery, with the bowel passing over it. The second plate was placed across the bowel at this point, and the two plates bound together near their ends. The interval left between them because of the rubber coverings over the ends allowed sufficient room for the intestine, tightly compressed, but not strangulated, to pass through. By bending the plates in or out the degree of obstruction was accurately regulated. We found by experience that the proper degree was obtained when the thin handle of a scalpel could just be passed within the bite of the plates, but not through it. (See Fig. 1, *b*.)

No. 19. The first dog on which the clamp was used was a male, weighing 13.5 kgm. He had been in the laboratory seventy-two hours without feeding, and had been given only sterile water to drink. This was done with the idea of getting the stomach and upper intestine as nearly free from bacteria as possible. Cushing and Livingood[20] have shown that the number present can be reduced very markedly in this way. The clamp was placed 18 cm. below the pylorus. The dog remained in excellent condition for five days following the operation. The temperature ranged from 37.5° to 38.5° C. and the pulse from 132 to 150. He drank freely of sterile water, which he vomited soon afterward, washing out bile and mucus with it. He passed small quantities of urine, which contained traces of bile and albumin. During this period he lost 1.8 kgr. He showed no active symptoms of the disease, and was in no apparent pain. The abdomen was not tender to palpation, nor was it distended. At operation the circumference of the abdomen was 47 cm. and on the fifth day only 43 cm. After the fifth day he began to show marked weakness and a more rapid loss of weight. The pulse and temperature remained about the same, and no new active symptoms developed. On the seventh day he was markedly weak and walked with difficulty. Emaciation was marked, there having been a loss equal to 19 per cent. of his body weight. He was killed with chloroform one hundred and seventy-two hours after the operation and the autopsy, with bacterial examination, immediately done.

[20] Johns Hopkins Hosp. Rep., vol. ix.

The obstruction was tested under water pressure, and was found complete, no water passing through the clamped point. Coils of intestine and omentum were matted around the clamp. On separating these, a small local abscess of green odorless pus was opened. The peritoneal coat of the intestine, at this point, was eroded by pressure, but no serious damage was done to the rest of the wall. The general peritoneal cavity was entirely free from evidence of inflammation. The liver and kidneys showed a marked congestion. There was a marked dilatation of the stomach and upper intestinal segment, and both contained water with bile and mucus. Their mucosæ were markedly congested.

Microscopic Examination. The intestine proximal to the clamp shows intense congestion and considerable exudative inflammation of the subserous tissue. The submucosa shows hemorrhagic and leukocytic infiltration. There is an acute hyperplasia of the lymph follicles. Distal to the clamp the intestine is normal. The kidneys show intense capillary congestion, especially of the glomeruli. The epithelium is not well preserved.

The spleen shows congestion.

The pancreas is normal.

The liver sections were unsatisfactory.

The cultures from the abscess around the clamp showed a pure culture of a Gram-negative bacillus, having the characteristics of colon bacillus. Cultures taken from the inside of the intestine, just above the clamp, showed the same bacterial growth, and in addition, a gram-positive coccus. Our effort to sterilize the upper bowel was not successful, and the local abscess probably resulted from the passage of organisms outward through the intestinal wall, where the peritoneal coat was damaged by the clamp pressure. Other organs were sterile (see table).

No. 20. Dog. Weight 9.5 kgr. No food for one hundred hours. Sterile water during this time. Repetition of No. 19. Post-operative symptoms the same. Lived ninety hours. Autopsy (five hours postmortem during which time the body was on ice) showed no peritonitis. Obstruction complete. Stomach a little dilated. Bowel above clamp twice the normal size. In the intestine, distal to the clamp were seen many hemorrhagic points.

Microscopic Examination. Intestine proximal to clamp shows fibrinous peritonitis, marked congestion of all coats, and exfoliation of lining mucosal cells. Stomach normal.

Liver. Congestion. Moderate granular and fatty degeneration.

Kidney. Moderate congestion. Tubules show granular coagulum. Cells swollen and show marked granular degeneration. Some cells show partial necrosis.

Cultures from femoral blood, peritoneum and liver show neither aërobic nor anaërobic growth.

No. 21. Puppy. Weight 8 kgr. Fed four hours before operation. Clamp applied 16 cm. below pylorus. The stomach contained food and the lymphatics and vessels were distended from full digestion. The post-operative course was the same as in the others. Pulse, 190. Temperature, 39° C. He died fifty-eight hours after operation. Autopsy, eight hours post mortem, the body being on ice. No peritonitis. Moderate distention stomach and duodenum. Few drops of purulent looking fluid around clamp, buried in adhesions. The obstruction was complete. The gastric and intestinal mucosa, proximal to the clamp, showed very little change. Distal to the clamp there were areas which resembled submucous hemorrhages in the intestinal wall. The other abdominal organs appeared normal.

Microscopic Examination. Proximal intestine not examined. Distal intestinal mucosa shows hyperplasia of lymph follicles, but no hemorrhages.

Liver. Marked congestion.

Kidney. Congested. Tubule cells swollen, and in places intensely degenerated. Apparent necrosis present in some foci of the tubules.

Spleen and pancreas much congested.

Bacteriology. Cultures from femoral blood, peritoneum and liver all sterile, both aërobic and anaërobic, with exception of one colony on one peritoneal aërobic slant agar tube. This showed pure growth of a Gram positive coccus and probably was an air contamination, one of the three found in the whole series.

No. 22. Bitch. Weight 10.25 kgr. Fed eighteen hours before operation. Clamp applied 12 cm. below pylorus. This animal was killed on the twenty-first day, up to which time she had showed no symptoms of suffering or of disease, except for loss of weight to 7.4 kgr. During this time she had eaten nothing. She drank water freely, however, for the first three days. After this she received 150 to 250 c.c. of normal saline solution subcutaneously, and then she refused water to drink. She only occasionally vomited. The temperature ranged between 37° and 38° C. The pulse for the first four days was around 130. It then became slower and during the last two weeks was between 70 and 100. Urine was passed freely and contained bile and albumin in small quantities. Several blood-cell counts were made during the later days of the experiment and the red cells numbered between 5,240,000 and 7,000,000, nearly all counts being slightly over 5,000,000. Killed with ether on the twenty-first day while still in good health. Autopsy. No peritonitis. Clamp allowed minimal drainage into gut below (compare No. 27). Stomach and duodenum were somewhat dilated and the intestine distal to clamp was contracted, showing very little flow into it. However, it contained bile, and under pressure water was forced through clamp into

bowel below. The mucosa of intestine and stomach appeared normal. The kidneys and liver showed congestion.

Microscopic Examination. Stomach and intestine not examined.

Kidneys. Tubules filled with granular coagulum. Cells show swelling and granular degeneration.

Liver. Intensely congested.

Spleen. Congested.

Pancreas. Normal.

Bacteriology. Neither aërobic nor anaërobic growth on tubes from femoral blood, liver or spleen.

No. 23. Dog. Weight 11 kgr. Starved five days, receiving only sterile water. Clamp applied 20 cm. below pylorus. He was killed on the tenth day. His symptoms were the same as in cases above. He received saline subcutaneously with apparent benefit. Pulse, 132 to 150. Temperature, 37.9° to 39.2° C. Weight at death 8.5 kgr. Urine contained albumin and bile. An extensive noma developed on face which accounted for high temperature. Autopsy immediately after death by cyanide. Obstruction complete. Stomach and proximal gut much dilated. Distal gut collapsed (Fig. 3). They contained about 300 c.c. of bile, mucus, and water. The specimen was preserved intact so the mucosa was not seen. No peritonitis. Liver and kidneys much congested. The latter showed acute degeneration, the markings being indistinct and the papillæ pale.

Microscopic Examination. Kidneys show granular degeneration, in places very marked.

Liver. Intensely congested. Considerable fatty and granular degeneration.

Spleen and pancreas show congestion.

Bacteriology. Aërobic and anaërobic cultures from femoral blood and liver were all without growth.

No. 24. Small bitch. Weight 6 kgr. Fed seventy-two hours before operation. Clamp applied 16 cm. below pylorus. Lived two hundred and five hours—a little less then nine days—with symptoms as in other cases. Pulse, 120 to 180. Temperature average, 39° C. Received saline injections throughout. Red-blood cells increased from 5,000,000 before operation to 6,720,000 on eighth day showing some loss of water. Weight 4.9 kgr. Died during night. Autopsy at 10 A.M. in morning. Obstruction complete as tested by absence of bile in distal gut, although under pressure, water could be forced beyond the clamp. No peritonitis. Around the clamp in a mass of omentum there was a collection of dirty yellowish fluid. The intestinal wall showed some damage within the bite of the clamp (see microscopic examination). The stomach and proximal intestine were moderately dilated, and contained a small amount of bile and mucus. The mucous membrane of the whole tract appeared normal to gross examination, as did the kidneys and liver.

Microscopic Examination. The intestine within the clamp showed an advanced purulent peritonitis, destroying longitudinal muscular coat. Congestion of mucosa. Exfoliation of epithelium.

Kidney. Congested. Tubules filled with granular coagulum. Cells swollen and show marked granular degeneration in places approaching necrosis.

Liver. Section lost.

Pancreas. Marked congestion.

Bacteriology. Aërobic and anaërobic cultures from femoral blood, peritoneum, and liver showed no growth. A Gram positive coccus was obtained in pure culture from the abscess around the clamp in all tubes both aërobic and anaërobic. This was undoubtedly an infection passing through the gut wall where the clamp damaged it, since the same organism was isolated from the intestine.

No. 25. Dog. Weight 6 kgr. Fed twenty-seven hours before operation. Clamp applied 16 cm. below the pylorus. He took ether badly and made a poor recovery. He was not given the hypodermoclysis of normal saline solution. Condition seemed good the next day. Died that night. Autopsy not done until day following, about thirty hours post mortem. Obstruction complete under water pressure. No peritonitis. Stomach and proximal gut somewhat distended. Distal gut collapsed. Mucosa of stomach and proximal gut markedly congested. Liver, spleen, pancreas, and kidneys showed congestion.

Microscopic Examination. Stomach congested. Proximal intestinal mucosa shows intense congestion. Marked round-cell infiltration of tips of villi and exfoliation of cells.

Liver. Intense congestion. Considerable granular and fatty degeneration.

Kidney. Not examined.

No bacteriological examinations made because of delayed autopsy.

No. 26. Bitch. Weight 7.2 kgr. Exact duplicate in every way of No. 25, except that she received the saline injections daily, the first one of 150 c.c. being given at the close of the operation. She lived ten days, and showed the same symptoms as in other dogs described. There was a marked contrast to dog No. 25, which did not receive the saline. Killed with ether and autopsied immediately. Obstruction complete against a column of water 90 cm. high. No peritonitis. The stomach and proximal gut were dilated to about three times normal. The mucosa of stomach and proximal intestine were congested. The liver, kidneys, and spleen were congested.

Microscopic Examination. Proximal intestinal mucosa shows intense congestion and exfoliation of living cells.

Kidney. Shows congestion. Tubules contain coagulum and

occasional blood cells and show granular degeneration, in places very marked.

Liver shows intense congestion, atrophy of liver cords about distended capillaries and moderate granular degeneration.

Spleen shows much hypertrophy of the follicles.

Pancreas normal.

Cultures from femoral blood, liver, spleen, and peritoneum were taken. These were all without growth after four days, under both aërobic and anaërobic conditions, except one aërobic tube (four were taken) from the liver. This showed one colony of Gram positive cocci growing well to one side of the stroke of the loop.

No. 27. Bitch. Weight 11.5 kgr. Fed twenty-eight hours before operation. Clamp applied about 15 cm. below the pylorus. Lived twenty-four days with only moderate development of symptoms during first week. Then behaved like a normal dog. Re-operated upon on July 20. The clamp was not sufficiently tight to make a complete obstruction (compare with No. 22). It was tightened and the next day it had cut its way through the gut wall and the dog died of a peritonitis.

No. 28. Dog. Weight 6.5 kgr. Fed twenty-eight hours before operation. Clamp applied 11 cm. below pylorus. Post-operative course as in other cases. Died in fifty-six hours and body immediately placed on ice. Autopsy ten hours later. Obstruction complete. No peritonitis. Local infection around the clamp. Stomach and proximal intestine only slightly distended and contained a small amount of bile-stained fluid. The distal gut was totally empty. Two superficial ulcers were seen in the mucosa of proximal gut. The liver, kidneys, spleen, and pancreas appeared normal.

Microscopic Examination. Intestine not examined.

Kidney. Tubules swollen and show granular degeneration, very marked in places.

Liver. Intensely congested.

Bacteriology. Cultures from the femoral blood, the peritoneum, the liver, the spleen, and the local collection of fluid around the clamp all were without growth under aërobic and anaërobic conditions.

No. 29. Dog. Weight 8 kgr. Fed thirty hours before operation. Clamp applied 11.5 cm. below pylorus. Post-operative course same as in other cases. Received about one-fortieth of body weight of normal saline subcutaneously daily. He remained in excellent condition for eight days, during which time he lost a little over 2 kgr. in weight. He drank water each day which was always vomited. Pulse from 130 to 174. Temperature, 38.5° to 40° C On the ninth day he was etherized and the abdomen opened. The obstruction was complete. The stomach and proximal intestine were much distended (Fig. 2), and filled with a greenish fluid of the thickness of pea soup. There was no peritonitis. The

splanchnic vessels were not much dilated, except those above the occlusion. The spleen was not enlarged. The liver and kidneys did not show much congestion. Sections were taken from the stomach, duodenum, distal intestine, liver, spleen, and kidney while the dog was still under ether, after which he was killed.

Microscopic Examination. The stomach is normal.

The proximal intestine shows marked congestion and an edema in the submucosa. The lesions here were not advanced, because the specimens were taken some hours before the animal would have died from the disease. The distal intestine is normal.

FIG. 2.—No. 29. Showing mucous surface of intestine at site of clamp. Note absence of damage to mucosa at this point and the congested appearance proximal to it. Also distention of duodenum above the clamp.

The liver is congested. The cells show granular degeneration and areas of necrosis are present.

The kidney is congested. Tubules contain granular coagula. The cells show granular degeneration.

The above series includes experiments on 11 animals which may be summarized. In 2 a complete obstruction was not obtained because the clamp was not sufficiently tight. These 2 animals were killed after twenty-one and twenty-four days respectively, while each was in good condition. They had emaciated a good deal, and one of them was weak, but otherwise they acted like normal dogs.

The remaining 9 dogs all showed a similar condition while living, and autopsy yielded the same findings in the organs. In some

dogs, particularly those which lived the longest, the dilatation of the stomach and the duodenum was very marked (Fig. 3, of No. 23).

Four dogs in this series were given sterile water by mouth only, and this they promptly vomited. They were, therefore, practically getting neither nourishment nor water, for if what they drank was not all vomited, very little absorption could take place from the stomach and duodenum. Beginning with the fourth dog, each dog

FIG. 3.—No. 23. Showing clamp in situ. Stomach and duodenum dilated. Vessels engorged.

received from 150 to 300 c.c. sterile normal saline solution, either subcutaneously, or by rectum, per day, and this was absorbed. In one case this was not given till the third day. This animal had then begun to act sick, but showed a marked improvement after the administration of the hypodermoclysis. In general, the dogs who received this saline, lived longer than the others. They sometimes drank sterile water in addition, but this they always vomited in a very short time. In many cases they refused to drink more than a few cubic centimeters. The 3 dogs which lived the longest

were all given the saline subcutaneously, and there seems no doubt that this procedure was very beneficial.

We attempted, by a count of red-blood cells, to determine whether the dogs not receiving it suffered from dehydration, with a consequent increase in the number of red cells per cm. There was not a sufficient variation from the normal, to throw any light on this point, the number ranging around 6,000,000 both before and after the saline injections. The saline may have acted in either of two ways. It may have prevented an actual dehydration of the tissues, which is a deleterious condition in itself, or it may have acted as a diuretic and thus aided the elimination of poisons by the kidneys. The longest post-operative life was ten days (2 dogs); a third dog lived just under nine days; the shortest period was thirty-six hours in a small fox terrier who never completely recovered from the operation. The average length of life was one hundred and thirty-nine hours in this series, as against sixty-seven hours in the series where the obstruction was produced by sectioning the intestine and inverting the ends, but it was only in the former that the aid of the saline injections was used.

It was, moreover, remarked that the second series in which no damage to the intestinal wall was produced was much nearer the normal throughout the experiment than was the first series in which the intestine was sectioned. So far as we know, no other experimenter has paid the same attention to producing an obstruction without any damage to the intestinal wall. There is evidence that the method is of advantage in excluding the complications which may arise from such damage. Clinically, we know that when a strangulation—however limited in extent—is superimposed on an obstruction, the course of the disease becomes much more acute. Medowoy,[21] Kocher,[22] and others, emphasize this point.

Murphy and Vincent[23] in their experiments, worked particularly on this phase of the question. In a simple obstruction in cats they found the intestinal wall very little damaged in four to six hours. When, however, the circulation was disturbed, particularly a venous stasis produced, a very severe change was present at this time. They conclude that "Interference with the circulation of the obstructed intestine is the vital factor in the production of the symptoms of ileus."

When the intestine is sectioned, and the proximal end sufficiently inverted to prevent the stomach and duodenal contents being forced through it, a local strangulation takes place. At autopsy there was always found in these cases a local damage to the intestinal wall at the inverted point, small in extent to be sure, but nevertheless sufficient to be the possible site of the absorption of

[21] Deutsch. Zeitsch. f. Chir., cv, S. 1.

[22] Mitteil. Grenz. d. Med. u. Chir., Band iv, Heft 2.

[23] Loc. cit.

a considerable amount of poison. Often, too, a very considerable intussusception of the invaginated stump was present. This mechanical damage, of course, is not an essential in producing death, because it was not present in the second series, and they died. We feel, however, that it has an important bearing on the problem, as we shall later, more fully explain.

We desire to call particular attention to the microscopic findings in these cases. The intestinal mucosa, proximal to the obstruction, shows a marked congestion. Marked round-celled infiltration is present, and exfoliation of the lining cells. Hemorrhages are often seen. There is present an acute hyperplasia of the lymph follicles. The submucosa is edematous. Distal to the clamp there is no change, or only a very slight change from the normal. The gastric mucosa shows only a congestion. The kidneys are markedly congested. The tubules contain granular coagula. The tubule cells are swollen and the seat of granular degeneration; not infrequently necrotic areas are seen.

The liver is congested and the cells show granular and fatty degeneration. Necrotic areas may be present.

The spleen shows marked congestion, and some hyperplasia of the lymph follicles.

The pancreas shows only congestion.

The above changes are those seen in many forms of toxemia, both bacterial and non-bacterial. They are found in the toxemia of starvation, of pregnancy, of delayed chloroform poisoning (Howland and Richards[24]), and of many of the acute infectious diseases. They are, therefore, very strong evidence that in our dogs, some toxic substance was present in the circulating blood during life. The rapid emaciation, the progressive weakness and the high pulse rate, with a comparatively normal temperature, all support this evidence. The two cases, Nos. 22 and 27, in which the obstruction was not complete, indicate that the condition is not one of simple starvation, because these animals received no food and practically no water to drink (the saline was given subcutaneously as in the others) during a period of over three weeks, and yet remained in a condition of good health. They showed less emaciation and loss of strength during the experiment than did the fully obstructed dogs in one-third as long a period.

In order to test this point still farther, however, a dog was kept in the laboratory for two weeks, and received absolutely no food or water by mouth. The saline injections were given daily. Under this treatment he remained in an apparent condition of perfect health. He lost 29 per cent. of his body weight. There was no evidence of weakness. The pulse rate was from 70 to 120, and the temperature normal. A second dog had the clamp applied to the

[24] Jour. Exp. Med., 1909, ii, 344.

pylorus. He remained well (Fig. 4) for fifteen days, receiving only the subcutaneous saline injections. The toxemia of starvation is, therefore, not the determining factor in producing the symptoms or the pathological changes found in intestinal obstruction. We attempted, as mentioned above, to eliminate a bacterial origin, either direct or indirect, for the toxic substances, by withholding food from the dogs and allowing them only sterile water to drink, both before and after the operation, with the hope that we might produce a sterile condition of the stomach and duodenum above the occlusion. In this we were not successful, for in the 6 cases where a bacterial examination of the intestine above the clamp was made at autopsy an abundant growth of the usual intestinal flora was found. A

FIG. 4.—Dog with clamp on pylorus. Showing good condition after twelve days. Examination under ether on the fifteenth day, while the dog was still in good condition, showed the clamp to be tight.

further attempt to accomplish such sterilization was done in two cases (Nos. 30 and 31) by producing an intestinal fistula just distal to the duodenum (Fig. 1, *c*). We hoped by gastric and retrograde washing through this tract to get it clean and then obstruct it. Both dogs, however, died within a few days, and no further attempt in this direction was made.

We then turned our attention to an elimination of the bile, pancreatic, and duodenal secretions as a source of the poisons. To this end, in five dogs (Nos. 32 to 36) the following operation was done (Fig. 1, *d*). The pylorus was divided and the two cut ends closed by inversion. The intestine was divided just distal to the

duodenum, and the proximal end implanted in the jejunum about 30 cm. lower down. The distal end was implanted into the stomach. By this means the stomach emptied into the intestine just below the duodenum, and the bile, pancreatic, and duodenal secretions passed into the jejunum about 30 cm. distal to this. Our intention was to cause an obstruction with the clamp, just orally to the new duodenal outlet when the animals should have recovered from the anastomoses, thus having an obstruction of the stomach and about 30 cm. of intestine, but not of the duct-bearing portion of the tract.

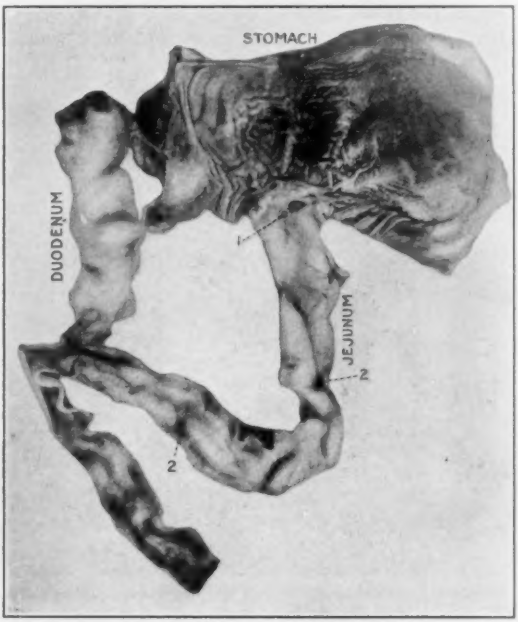

FIG. 5.—Showing damage to jejunum where the gastric juice passes into it without neutralization by entering duodenum; 1, perforation just below gastrojejunostomy; 2, ulcerations lower down.

For a few days following the operation these dogs did well, fully regained their appetites and seemed to be in good health. After about a week, however, they all began to act sick. They did not eat well, and sometimes vomited. They lost weight rapidly. Some of them developed diarrhea with bloody appearing stools. Four of them died in about four weeks with evidence of malnutrition. The autopsy showed, in two of these, that a very extensive damage to the intestine between the stomach and duodenal anastomosis was present. Ulcers were seen which were about to perforate (Fig. 5).

The stomach and this part of the gut contained partially digested blood.

The fifth dog seemed to be in fair condition after two weeks and on the nineteenth day the abdomen was opened under ether anesthesia. The anastomoses were satisfactory and no evidence of ulceration was present from the peritoneal surface. The occlusion clamp was applied just above the anastomosis of the duodenum with the jejunum. The following day the dog was in good condition; he had not vomited. He was given saline subcutaneously.

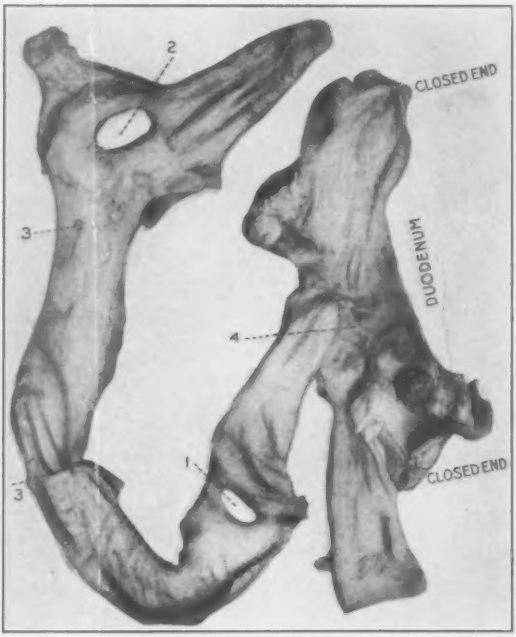

FIG. 6.—Showing perforation: 1, at site of clamp where it was applied nineteen days after anastomosis; 2, gastrojejunostomy stoma; 3, artefacts; 4, duodenojejunal anastomosis.

He died during that night and autopsy was done in the morning. The anastomoses were satisfactory. A general peritonitis was present from a perforation within the bite of the clamp (Fig. 6). The stomach and intestine anastomosed to it were distended with a dirty brownish fluid. On opening them the gastric mucosa was seen to be much congested; the mucosa of the jejunal segment was markedly congested and contained many hemorrhagic areas. The occlusion clamp had caused a perforation through one of these areas. The intestine below the duodenal anastomosis was entirely

normal in appearance. Similar ulcerations have been observed in the jejunum of dogs, after a long loop anastomosis to the stomach, by Exalto,[25] and many clinical cases of jejunal ulceration are reported following gastro-enterostomies.

Our attention was attracted by these cases to the damage done to the intestinal wall when the gastric juice unneutralized by the duodenal secretions comes into contact with the intestinal mucosa. Our effort to produce an obstruction in which the duodenal contents should not be stagnated had not been successful. But the symp-

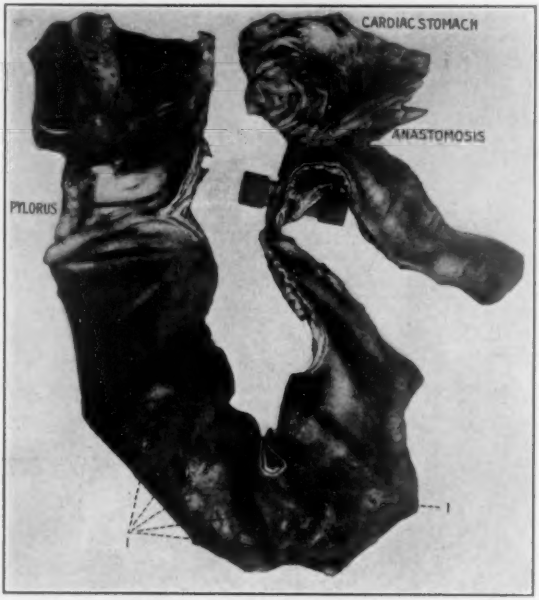

FIG. 7.—Showing perforation (1) and ulceration (2) in doubly occluded stomach and duodenum.

toms developing in these dogs and the findings in the intestinal mucosa turned our attention in another direction which we think led to important results. In many ways these dogs behaved like the ones with an obstruction, the symptoms and the course of the disease being, however, much less acute. The microscopic examination of the intestinal mucosa, the kidneys and the liver showed, too, the same lesions as found in the simple obstruction. It, therefore, occurred to us that the damage we had noted in the mucosa, above the occlusion, might be a factor in the production of the

[25] Mitteil. Grenzgeb. d. Med. u. Chir., 1911, Band xxiii, Heft 1.

toxemia which caused the animal's death. To further test this point, the following experiment was done three times (Nos. 37 to 39).

The stomach was bisected and the two cut ends closed. A gastro-enterostomy was made between the cardiac half of the stomach and the first part of the jejunum. The occlusion clamp was then applied just proximal to this anastomosis, or the proximal end of the divided jejunum was implanted into the pyloric half of the stomach. In this way the secretions from the pyloric half of the stomach, the liver, the pancreas, and the duodenum were occluded within half of the stomach and the duodenum (Fig. 1, *e*). Two of these dogs died in approximately thirty-six hours; one in eighteen hours. They were very sick during this time. The pulse was 200 and over. They vomited. At autopsy the occluded portion was found enormously distended with a mixture of bile and mucus which was blood tinged. The stomach and intestinal wall were markedly stretched, the latter to paper thinness. In one case, at a point near the lower end of the duodenum, an ulcer was present which had perforated through the peritoneal coat, and around it was an area of necrosis 5 cm. in diameter. Proximal to this point were five extensive ulcers (Fig. 7). The mucosa throughout was markedly congested. In the other 2 cases no ulceration was seen, but the damage to the mucosa was very severe. In the jejunum, immediately below the gastric stoma, the mucosa was damaged in a similar way to that seen in the previous series, due to the unneutralized gastric juice entering it. Microscopical examination of the tissues gave the same findings as in the obstructed cases.

In the next series of experiments, Nos. 40 to 43, a loop of intestine below the duodenum was occluded by sectioning and closing the ends, or by the use of the clamps, and the patency of the tract reëstablished by an anastomosis between the proximal and distal arms, above and below the clamps (Fig. 1, *f*). One was done high up in the jejunum, two in the middle of the small intestine, and one just above the cecum. The first of these dogs lived about eighty-jour hours, and during the first three days of this time he seemed perfectly well. He drank water and took food without vomiting. He suddenly began to act sick on the fourth day and died that night. The closed ends of the loop were not tight, and leakage had taken place, resulting in peritonitis. The occluded loop showed an intense congestion and it was distended with dark bloody fluid. The mucosa showed hemorrhagic areas. The peritonitis, however, renders the case useless except for a study of the damage done to the occluded loop.

In the second case, leakage in a similar manner also took place, vitiating the result so far as the course of the disease is concerned. The occluded loop, however, was much distended with a thin

bloody fluid. The mucosa was markedly congested and at one point a superficial erosion was present.

The third dog, in which the occlusions were done with the clamps, lived about one hundred and ten hours. He remained well for three days, and then began to show marked symptoms similar to those seen late in the obstructed cases. Autopsy. The anastomosis was tight and the clamps had produced a complete closure. There was no abnormality seen in the alimentary tract, except in the occluded loop, which was 44 cm. in length and began 76 cm. below

FIG. 8.—Showing distended nearly gangrenous loop of intestine after double occlusion in upper jejunum. Rubber tubes indicating points at which clamps were placed; (1) entero-enterostomy. Mesenteric vessels perfectly patent.

the pylorus. This loop was enormously distended and contained about 500 c.c. of a bloody exudate containing granular material resembling hashed up blood clot. The loop was nearly gangrenous[26] throughout the whole extent of its convexity, the process being much more marked in the outer coats than in the mucosa (Fig. 8). No localized ulcerations were seen. The mesenteric vessels were filled with fluid blood, showing that gangrene did not result

[26] Cf. Roger and Garnier, loc. cit.

from their thrombosis. The gastric mucosa was not congested, but that of the duodenum was slightly so. The kidneys and liver showed a very marked congestion.

The fourth dog in this series had the clamps applied in the lower ileum, closing off a portion of the bowel about 25 cm. in length, proximal to the cecum, with an anastomosis between the proximal and distal arms. He was an old animal, nearly blind, and a poor operative subject. For three days he remained in fair condition. He drank water and did not vomit. The pulse was about 150 to 170 and the temperature 40° C. On the fourth day it was noted that the wound was badly infected, and he began to suffer from the dyspnea which is so often seen in old dogs. Ether was given and the abdomen reopened. The wound was badly infected, and a large intramural abscess was present. There was no peritonitis. The anastomosis had not leaked. The clamps were tight. The occluded loop was not distended. It contained only a few cubic centimeters of dirty brown mucus. The mucosa showed no evidence whatever of congestion. The condition was in marked contrast to that seen in the over-distended, ulcerated and gangrenous loops of the upper tract. The sickness of this dog we attribute to his age and general condition before operation, and to the severe infection in the wound, more than to the occlusion itself. McClure[27] and v. Baracz[28] have found similar results to this. They are to be explained by the absence of any irritative agents in the occluded lower ileum loop which cause damage to the mucosa. Hence, no poisons, bacterial or otherwise, are able to pass the defense of the lining cells and the animal remains unpoisoned (cf. occlusion of pylorus, page 388). The experiments of the last two series demonstrate that when, in a dog, any portion of the upper small intestine, either alone or with a part of the stomach, is occluded at both ends, and the patency of the alimentary tract reëstablished by an anastomosis, the animal lives even a shorter time than in the simple high obstruction. He rapidly develops symptoms which come on only late in the obstructed dogs. The occluded loop is always markedly distended, and its wall is severely damaged by ulcerations or by destruction of the mucosa, and the damage may go on to gangrene. There is hemorrhage in the loop. If the loop receive the active digestive juices the damage is most marked in the mucosa; if it be lower down, the process is most marked in the outer coats. The vessels in the mesentery are not thrombosed, though an examination of the gut wall suggests this as a cause of the lesion. In the lower ileum the damage after four days may be very slight. If these lesions be compared to those already described as appearing in a simple high obstruction, they are seen to be of the same character, though much more severe. They resemble also the lesions

[27] Loc. cit. [28] Loc. cit.

produced when the gastric juice unneutralized by the duodenal contents is emptied into the jejunum. From these findings it would seem that in all our experiments a destructive agent was at work which seriously affected the mucosa of the intestinal wall.

As is well known, one of the functions of the intestinal mucous membrane is to so alter the substances which pass through it into the blood, that they are not toxic to the organism. The changes which we have found in the structure of the mucosa, we believe, deprive this membrane to a greater or less extent of this function, and in consequence the toxic substances, which other workers have demonstrated to be present, actually enter the blood in their poisonous condition. If the damage to the mucosa is great as in double occlusion, the poisons enter the system rapidly, and the course of the disease is short. If the damage is less severe, as in simple obstruction, where oral drainage by vomiting can take place, the course of the disease is lengthened. Therefore, change in the intestinal mucosa, proximal to the obstruction, is to our minds, the key to the solution of the cause of death in intestinal obstruction. This change results from the irritating influence of the retained digestive juices, and the mechanical damage due to the stretching of the intestinal wall. It deprives the mucosa of its defence against the passage of substances which are poisonous to the organism. These poisons, therefore, slowly enter the blood, and work the damage seen in the kidneys and liver, and ultimately produce the death of the animal. The poisons are present in the normal stomach and intestine,[29] and it is not necessary to consider that the obstruction causes any alteration in them. Abnormal absorption is the essential factor.

This explains the total lack of symptoms observed in our dogs over a period of nearly a week in some cases. The changes in the mucosa of the intestine were not sufficiently great to deprive it of its defence against the passage of unaltered poisons (No. 23). When the change once developed, this abnormal absorption took place rapidly, and active symptoms ending in death soon resulted. The subcutaneous injection of saline was beneficial because it probably aided in the elimination of the poisons by the kidneys, as well as prevented a dehydration of the tissues from lack of water. Any method of producing the obstruction, which causes a mechanical damage to the intestinal wall, hastens the development of symptoms and death, because the defence is then locally broken down. We see in this an explanation of the much more severe type of the disease when a strangulation is superimposed on an obstruction.

In one dog the clamp was applied directly to the pylorus. This animal lived in a condition of good health for fifteen days (Fig. 4).

[29] Roger and Garnier, loc. cit.

During the first twelve days he received the saline injection subcutaneously and refused to drink any water. His condition remained so nearly normal that it was concluded that the clamp was not causing a complete obstruction. The saline injections were discontinued, and he was given water by mouth and 50 grams of chopped beef heart on the twelfth day and 75 grams on the thirteenth day. The next day he refused to eat anything more, but he drank water freely, some of which he vomited. On the fifteenth day he was etherized and the abdomen was opened. The clamp was found to have caused a complete obstruction. There was no peritonitis. The stomach was enormously dilated, filling nearly the whole abdomen. This dilatation had occurred only during the three days in which he received water by mouth, as determined by the measurement of his girth which increased from 30 cm., the normal size, to 50 cm. The contents of the stomach was water with remnants of finely digested meat. The mucosa was entirely normal in appearance. There was no congestion of any of the abdominal viscera. From this experiment it is evident that the gastric juice, when stagnated in the stomach itself, is not absorbed as a toxic substance, so long as the mucosa remains normal. As shown, however, in experiments 32 to 36, it produces changes in the small intestine, when unneutralized by the duodenal contents which permit the absorption of materials producing symptoms and pathological lesions in the organs analogous to those of an obstruction. These facts are very strong evidence that the damage to the mucosa occurring in ileus is a necessary factor in the production of the toxemia there seen.

The following is a summary of the findings of our work:

1. A high intestinal obstruction, that is, 10 to 30 cm. from the pylorus, in dogs, may not produce death for ten days, provided the gut wall is not damaged. If it is damaged by section and inversion the average life is only half as long.

2. There are found in the kidney and liver cellular changes which are the same as those found in many toxic diseases. The intestinal mucosa is found to be damaged to such an extent that it may readily be conceived that it has been deprived of its natural defence against the passage of toxic substances, unaltered, through it.

3. Bacterial invasion of the blood and organs does not necessarily occur.

4. Dogs deprived of food for forty-eight to seventy-two hours, may die as early as those fed ten to twenty hours before the obstruction is produced. Decomposition of foodstuffs is not, therefore, an essential element in causing death.

5. If a double occlusion of the alimentary tract, with reëstablishment of the continuity of its lumen, above the lower ileum be produced, the damage to all the tissues is greater than with a simple

obstruction, and the course of the disease to a fatal termination is shorter. A double occlusion in the lower ileum produces much less damage than in the upper.

6. The action of the gastric juice, bile, pancreatic juice, and duodenal secretions are not a requisite in producing the symptoms and pathological changes seen in intestinal obstruction, because these are produced by a double occlusion in the upper ileum when none of these secretions are blocked.

7. Simple occlusion of the pylorus does not necessarily produce any evidence of a toxemia in two weeks, and the gastric mucosa at the end of this time shows no evidence of being damaged.

8. The above findings indicate that death from intestinal obstruction in dogs results from the presence of toxic substances in the circulating blood which produce fatal lesions in the kidney, liver, and other tissues. The essential factor which admits these substances into the blood is an injury to the lining cells of the intestine caused by the irritating action of the stagnated contents, together possibly, with the mechanical damage due to stretching. The poisons themselves may arise from the secretory activity of the various digestive glands, or from bacterial activity. They may be the same as those found in the normal tract or they may be substances newly formed under the conditions of stagnation. What ever their source, they are innocuous so long as the mucosa remains normal.

We desire to acknowledge our indebtedness to Drs. Ewing, Lusk, Elser, and Huntoon of the Cornell Medical College, not only for valuable advice and suggestion in this work, but also for material aid in carrying out the pathological and bacteriological investigations connected with it.

LOSS OF EMOTIONAL MOVEMENT OF THE FACE WITH PRESERVATION OR SLIGHT IMPAIRMENT OF VOLUNTARY MOVEMENT IN PARTIAL PARALYSIS OF THE FACIAL NERVE.

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The voluntary and emotional movements of the face are independent of one another, and one form may be lost without loss of the other. Von Bechterew[1] says a number of observations show

[1] Die Funktionen der Nervencentra, vol. ii, p. 1144 et seq.

positively that the emotional movements in man are accomplished by means of special tracts which have no relation to the tracts concerned with voluntary movement. Cases of paralysis are known in which voluntary movements of the face, or of the lower part of the face, were lost and emotional movements (laughing, crying) of the face were performed in a normal manner. In discussing these cases, Nothnagel remarked that when the voluntary movement of the face is lost in hemiplegia from a focal lesion, but both sides of the face take part in equal degree in emotional movement, one may assume that the optic thalamus and its connections with the cortex are uninjured. Cases in which the emotional movements of the face have been lost and the voluntary movements preserved have been reported by v. Bechterew, Nothnagel, Rosenbach, Kirilzew, Gowers, and many others.

According to v. Monakow,[2] it has long been known that in many cases of hemiplegia the face on the affected side cannot be moved voluntarily, but the paretic facial muscles at once contract, as well as those of the other side, when the patient laughs or cries. v. Monakow expresses his belief that a part of the sensory reflex tract for laughing or crying is situated in the optic thalamus.

The experimental work of Roussy[3] throws doubt upon the optic thalamus as a reflex centre for emotional movements of the face, as does the work of Ernest Sachs,[4] who, in the report of his experiments upon the optic thalamus states that stimulation produced facial movements of the opposite side. He adds: "It is desirable, perhaps, to repeat here that these motor phenomena constitute no evidence of special centres in the thalamus for automatic or rhythmic movements, as has been assumed by some authors." One possibly might make the objection that the results obtained in animals are not applicable to man.

Lewandowsky[5] believes the opinion regarding the optic thalamus as an emotional centre is not well founded. There are so many negative cases in the literature that a relation of paralysis of emotional movement to thalamic lesions cannot be maintained. Even in the cases in which thalamic lesions have been found, different parts of the thalamus have been affected. It is not improbable, he adds, that the assumption of a relation between emotional facial movements and a thalamic lesion is without foundation.

The paralysis of one form of facial movement without impairment or with only slight impairment of the other may result from a lesion of the facial nerve, or may be a pseudoparalysis from imperfect innervation. I have observed persons who in smiling or speaking innervated one side of the face so much less than the other that paresis of one side seemed to be present, and yet the drawing up

[2] Gehirnpathologie, Nothnagel's System.
[3] La couche optique, p. 185.
[4] Brain, Part 126, vol. xxxii, p. 1909.
[5] Allgemeine Neurologie, Part 2, p. 741 et seq.

of the corners of the mouth, as in showing the teeth, was equally good on the two sides.

FIG. 1.—In smiling, only the right side of the face showed contractions of muscles.

FIG. 2.—In showing the teeth, contractions of the muscles were only a little less pronounced on the left side of the face. The reproduction does not show these contractions so well as does the photograph. The photographs were taken after the operation. The dissociation of facial movements was more pronounced before the operation.

What I especially desire to call attention to at the present time is loss of emotional movement of one side of the face with preserva-

tion or possibly only slight impairment of voluntary movement of the same side, as indicative of a certain stage of peripheral facial palsy. I have observed this phenomenon especially in slight facial weakness resulting from the pressure of a tumor of the cerebellopontile angle upon the facial nerve. The movement of the face normally is less intense in smiling or crying than in showing the teeth, and, therefore, a slight paresis of the facial nerve might cause loss of these emotional movements on one side of the face, and the weakness might be overcome by the forcible effort made to contract the lower part of the face in showing the teeth. The case was one referred to me by Dr. W. H. Snyder and Dr. Louis Miller, of Toledo, Ohio, October 23, 1910. In smiling the man drew up the right side of the face strongly and the left side weakly, but in showing the teeth or drawing up the corners of the mouth separately, the left facial weakness was slight. Dr. C. H. Frazier operated and found a tumor in the left cerebellopontile angle pressing upon the facial nerve.

It is important to recognize that this form of dissociation of facial movement may be the first sign of weakness of the facial nerve from pressure of a cerebellopontile angle tumor, and in connection with slight nerve deafness may be of localizing value. It is possible that the impairment of emotional movement may result, in part at least, from the pressure of the tumor upon the medulla oblongata and pons. I am unable to determine at present whether or not the impairment of emotional movement of the face occurs in most cases of tumor of the cerebellopontile angle.

THE RELATIONSHIP BETWEEN ERYTHEMA NODOSUM AND TUBERCULOSIS, WITH THE REPORT OF A CASE.

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Erythema nodosum has been variously regarded as a simple variety of erythema multiforme, as a definite specific contagious disease (Paulouch, Oppert, Batigne et al.), and as a secondary manifestation in many differing conditions, such as the infectious diseases, drug ingestion, alimentary disturbances, and nervous diseases.

Jouillié divided erythema nodosum into two classes—primary or so-called idiopathic and those secondary to infectious diseases, certain drugs and nervous disorders. In 1872 to 1878 Uffelman and Oehme reported some observations from which they concluded that tuberculosis was frequently a cause of erythema nodosum.

Cases reported by Schmitz, Comby, Oppert, Goldscheider, Buisine, Levy, Schamaun, Poncet, and others, have shown an association between erythema nodosum and tuberculosis. More recently Troisier and Chauffard, in France, and Otto Brian, in Germany have discussed the correlation of erythema nodosum and tuberculosis. Mlle. A. Pérel in her "Thèse pour le Doctorat en Médecine" discusses the relationship between erythema nodosum and tuberculosis, citing a number of cases from the literature and from her own experience, in which there was apparently a definite connection between the appearance of the erythema nodosum and a concomitant or subsequent tuberculosis.

Hildebrandt injected 5 c.c. of venous blood, taken from patients suffering from erythema nodosum, into the peritoneal cavity of guinea-pigs and succeeded in producing tuberculous lesions in them. Otto Brian repeated the experiment of Hildebrandt and was able, in one case, to infect 3 guinea-pigs with tuberculosis by injecting them with the venous blood taken from a patient with erythema nodosum. In all the other cases, however, in which this experiment was tried, he failed to infect a single animal. Chauffard and Troisier were able to produce an experimental erythema nodosum by the "intradermic injection" of tuberculin in very small doses and this experiment has been repeated successfully by several workers, notably Marfan, Carnot, Widal, and Benard.

A number of observers have maintained that in patients afflicted with such skin lesions as erythema multiforme, urticaria and the like, a reaction analogous to that obtained with tuberculin could be produced by the intradermic injection of diphtheria antitoxin, tetanus antitoxin and even with normal salt solution. Mlle. Pérel, together with Chauffard and Troisier, controlled their intradermic injections of tuberculin by the simultaneous injection of salt solution and the various sera, and in all but one case the control injection gave negative results.

Landouzy, in 1907, at the Congress of the French Association for the Advancement of Science, maintained that erythema nodosum was a local manifestation of a bacillary septicemia.

Chauffard and Troisier, in their intradermic experiments, were able to produce at the site of injection a nodule which, in all of its characteristics, appeared identical with the nodes in erythema nodosum. They believed that this experiment was evidence in favor of the theory that the plaques of erythema nodosum resulted from the conflict between the tubercle bacillus in the circulation and the antibodies which are present at certain points in the organism.

Otto Brian was able to demonstrate, by means of sedimentation with acetic acid and antiformin, in the venous blood of patients afflicted with erythema nodosum, an acid-fast bacillus, but excepting in one case he was not able to produce tuberculous lesions in guinea-pigs by injecting them with the blood in which these acid-fast bacilli occurred. He obtained positive reactions to the injection of tuberculin and to the von Pirquet skin test, but he did not think that this gave any proof that the erythema nodosum was as such of a tuberculous nature.

He concludes that: (1) The etiology of erythema nodosum is not uniform. (2) Tuberculosis is by no means the only cause of erythema nodosum; in fact, it is the cause apparently only in a small percentage of the cases. (3) The assumption that each case of erythema nodosum represents a rheumatic infection in special form is not well founded. (4) The throat is the portal of entry for the infection in many cases of erythema nodosum, but not for all.

Mlle. Péral in her thesis reports 22 cases in which a definite relationship existed between erythema nodosum and tuberculosis. Among these cases were several in which there was an apparent association between the erythema nodosum and tuberculous meningitis.

We offer the following report of a case of erythema nodosum which occurred as an early manifestation in tuberculous meningitis:

On January 24, 1910, there was admitted to the wards of the second medical division of Bellevue Hospital, a young Italian woman, aged twenty-five years. There was nothing in the family history nor in the past history which had any bearing on the present illness.

Two weeks before admission to the hospital she noticed an eruption on either cheek, occurring first as discrete papules and vesicles which shortly coalesced to form a continuous patch. The only subjective symptom at that time was the slight itching which accompanied the eruption. A few days later there appeared on the arms and on the legs numerous bright red spots and on the anterior aspect of the legs several hard, raised nodules, which were excessively tender on palpation. With the appearance of these nodules the patient complained of a general feeling of lassitude, anorexia, fever and pains in the joints, especially in the knees. The chief complaints on admission were the eruption on the face and limbs, fever, malaise, and arthritic pains.

The physical examination on admission showed a well-developed and well-nourished young woman, aged about twenty-five years, who did not appear to be very ill. The temperature was 100.5°, the pulse rate was 96, the respirations 24 per minute. The skin over the cheeks and to a lesser extent over the forehead was reddened,

thickened and scaling. The right pupil was slightly dilated, both pupils reacted promptly to light. The conjunctivæ were normal. The tongue was thickly coated. The throat was normal. The tonsils were not hypertrophied. The teeth were in good condition, there was no pyorrhea. The cervical glands were somewhat enlarged.

The chest was well developed. The heart and lungs were normal. No masses were made out in the abdomen. The liver, spleen, and kidneys were not palpable.

The skin over the chest, back, and abdomen was clear. Over the extensor surfaces of the forearms, and especially marked in the vicinity of the wrist joints on either side, there were noted a number of discrete macules, violacious in color and irregular in outline, varying in size from that of a ten cent piece to that of a silver dollar. In some of these spots the color disappeared on pressure, while others were distinctly purpuric. Over the anterior aspect of the tibiæ and ankles an eruption similar to that described on the arms was seen and, in addition, over the thighs and legs and having no direct relation to the joints, there were noted several raised, red, sharply circumscribed nodules, varying in size and excessively tender on palpation.

The patellar reflexes were normal. There was no general glandular enlargement. Some tenderness was elicited by pressure over the lateral aspect of the knee-joints. There was no effusion into any of the joints.

The blood examination on admission showed: hemoglobin, 90 per cent.; white blood cells, 10,000; differential count: polymorphonuclears, 77 per cent.; lymphocytes, 17 per cent.; transitionals, 6 per cent.

The urine examination showed a specific gravity of 1034, no albumin, no sugar, no indican. On microscopic examination a few epithelial cells, a few white blood cells, and very rarely a hyaline cast were found.

The case then presented on admission: An erythema multiforme on the face and on the extremities accompanied by an erythema nodosum.

During the first three weeks of the patient's stay in the hospital there was no change in the condition. The temperature varied between 99° and 103° F. The eruption on the face gradually cleared up. During this time several crops of nodes appeared.

On February 18, twenty-five days after admission, the patient said that she felt well and that she desired to leave the hospital. No new nodes had appeared for several days. There was no longer any pain in the joints. The erythema had entirely disappeared and the purpuric eruption on the arms and legs was fading rapidly. Her malaise and anorexia had entirely disappeared, and her appetite was good. One symptom alone remained unchanged, namely,

the fever, which continued to run a remittent course, varying between 99° and 101° F. A blood culture made on February 24 was negative. On February 26 the patient complained of pain in the epigastrium. This was followed by persistent nausea and vomiting. She became drowsy and apathetic, taking no interest in her surroundings. An ophthalmoscopic examination at this time showed a perfectly normal fundus; there was no choking of the disks.

For the next week the nausea and vomiting continued, there was a total inability to retain food. The patient lost in weight rapidly. The temperature continued to be remittent in type. The pulse was rapid, irregular, and of low tension.

On March 2 the patient developed a slight cough, and on examination of the lungs at this time there was discovered over the base of the right lung behind, dulness on percussion, prolonged and high-pitched expiration, bronchial voice, and many medium moist rales.

A blood count done at this time showed: hemoglobin, 60 per cent.; white blood cells, 13,000; differential: polymorphonuclears, 74 per cent.; large mononuclears, 14 per cent.; lymphocytes, 11 per cent.; transitionals, 1 per cent. A spinal puncture was performed and 7 c.c. of slightly turbid fluid under moderate pressure were withdrawn. The report from the laboratory was that the fluid was "negative for tubercle bacilli." A cyto-count was unfortunately not made.

There was now a marked change in the patient's condition. She had become extremely restless; there was an almost continuous cephalic cry; the head was retracted and the neck was rigid. The pupils were dilated and irregular. A convergent strabismus was present. The ophthalmoscopic examination revealed a double choked disk. No tubercles of the choroid were observed. The face was somewhat flattened on the right side, the mouth was drawn to the left and the tongue deviated sharply to the right. A well-marked *tache cerebral* was present. A marked Kernig's sign was elicited. The patellar reflex on the left side was absent and diminished on the right side. The respirations had assumed the Cheyne-Stokes type. The pulse was rapid, weak, and irregular. On lumbar puncture 44 c.c. of clear fluid were obtained under considerable pressure and the presence of tubercle bacilli was demonstrated in this fluid. The patient died on March 10.

The autopsy findings were as follows: Tuberculous lymph adenitis of the cervical and mediastinal glands. Tuberculous bronchitis and bronchopneumonia involving the right lower lobe. Localized miliary tuberculosis of the right lung. Tuberculous meningitis. Brown atrophy of the heart. Parenchymatous degeneration of the kidneys. Otitis media involving the right ear.

ON CERTAIN CHANGES IN THE ELASTIC TISSUE OF THE PELVIS OF THE KIDNEY, AND THEIR RELATION TO HYDRONEPHROSIS.

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(From the Russell Sage Institute of Pathology.)

Inducement to this study was given by a frequent occurrence of a dilated pelvis of the kidney, which assumed at times extreme dimensions in cases of arteriosclerotic and senile kidneys, and in advanced productive nephritis. No extrarenal obstruction or anomalies of insertion or angle of the ureter could be discovered.[1]

In some of these cases the kidneys presented the picture of a long-standing, double hydronephrosis, although the extent of the lesion was at times different on both sides. In a number, particularly the aged, the lesion had become associated with an inflammatory condition of the pelvis, but only in a few it assumed a purulent character.

These observations extended over 505 autopsies performed during the year 1909. Among them were 15 which showed a marked dilatation of the pelvis of the kidney; in 3 this was complicated by a purulent pyelitis. In none was any common obstruction or abnormality in the relationship of the ureter to the pelvis discovered, which would account for retention of urine. The ureter was not dilated in these cases, but the walls of the pelvis of the kidney were considerably thickened. The urethra was found intact, and the walls of the bladder were not affected. In several cases the disease was not the same on both sides, and in some early instances parts of the kidney were still intact, while in others considerable flattening of papillæ had taken place with much distention of the calices. Below are cited the extreme cases:

Case I.—An emaciated man, aged seventy years, had died from lobar pneumonia of the upper and middle lobes of the right lung and pneumococcal meningitis. The heart (510 grams) was considerably hypertrophied, particularly the wall of the left ventricle. Urinary bladder and urethra presented no special change. The renal arteries were both somewhat atheromatous. The renal cortex was fairly well preserved. The right kidney (112 grams) was somewhat reduced in size, its capsule slightly adherent and thickened, its cortex irregularly reduced, and its vascular markings irregular as in the usual forms of arteriosclerotic atrophy of the kidney. The pelvis of this kidney was considerably distended

[1] An illustration of this disease will be found in my monograph, The Anatomic Histological Processes of Bright's Disease, Philadelphia, 1910, Fig. 45.

and its walls thickened. The left kidney was virtually transformed into a sac. Its pelvis was enormously distended and the kidney substance almost completely lost. Microscopically, what kidney tissue had remained showed the glomeruli almost completely overgrown with fibrous tissue, and the tubules obliterated. In some remaining tubules the lumen had become largely distended and their lining cells transformed into flattened epithelium.

CASE II.—An emaciated woman, aged eighty-eight years, had been under observation for progressive weakness and mental enfeeblement for six months. Her urine had been increased in amount and always presented a small amount of albumin and casts. Toward her end she became edematous and died of cardiac failure. Autopsy showed a heart of 300 grams, atrophic. There existed general arteriosclerosis. Both kidneys were considerably reduced in size (150 grams); the pelvis in both was markedly dilated and its walls slightly thickened. The urinary bladder was somewhat dilated and its walls thin and atrophic. There was no suppurative condition in any part of the urinary tract.

CASE III.—The third case presented much the same appearances, but had a superadded pyelitis. It occurred in a wasted male, aged sixty-nine years, who for one year had been progressively wasting, and had been recognized to have nephritis. There was a slight increase in the amount of urine with some albumin and casts, but never any pus. He died of gradual cardiac insufficiency. At autopsy the heart (300 grams) was atrophic, and there was a considerable degree of arteriosclerosis. The right kidney (150 grams) showed a moderate degree of arteriosclerotic atrophy, and the left (75 grams) was much reduced in size, while on section its pelvis was markedly dilated, and the calyces were so distended as to almost completely obliterate the kidney tissue. The pelvis was filled with a thick cheesy pus. Microscopically, no organisms were found, but the lesion was certainly not tuberculous. The ureters were patent and the urinary bladder was not hypertrophied nor did it contain any purulent material. There was a history of gonorrhea twenty years previously, but no apparent trace of this was determined at autopsy.

We deal, therefore, in this series with cases of hydronephrosis of all grades, from dilated calices to an almost complete obliteration of kidney substance and the formation of a large sac; some complicated by pyelitis; in all the direct cause of the lesion was obscure.

In a recent very extensive experimental and anatomical study of this disease, Ponfick[2] classifies it into two great groups, one with manifest, the other with obscure or doubtful etiology. Of a total number of 76 cases studied, 53 had a manifest cause, while as many

[2] Beiträge zur pathologischen Anatomie begründet von Ziegler, Band XV, Heft 1.

as 26 belonged to the latter and most interesting class. It is frequently asserted that hydronephrosis of obscure origin finds an explanation in a valve-like reduplication of a fold of mucous membrane at the junction of ureter with kidney pelvis. Ponfick, however, attributes such changes in the mucous membrane in infantile and in a certain number of cases of adult hydronephrosis to urinary concretions, which, having become lodged at the orifice of the ureter, produce urine stasis, and by irritative processes give rise later to the formation of an obstructing fold of mucous membrane, which persists even after disappearance of the concretion. In Ponfick's opinion the condition is, therefore, acquired and not developmental. There still remain, however, cases of obscure hydronephrosis without any such fold formation. Ponfick believes these due to an abnormal course of the ureter, producing an abnormal degree in the angle which the ureter forms with the pelvis of the kidney. Incidentally Ponfick mentions that the progress of the lesion may be aided by a gradual atrophy of the contractile elements which accompany the induration of the intermuscular connective-tissue bands of the pelvis. It does not appear that he attributes to these anatomical changes in the pelvis any essential role for the production of the hydronephrotic process.

The explanations of Ponfick are not applicable to the cases under consideration. In none of them were there evidences of previous concretions with changes in the mucous membrane or an abnormal angle or course of the ureter. Moreover, the irregularity in the development, as exemplified by early cases, its constant occurrence in diseases associated with slowly progressing atrophy of renal substance, and in the aged, suggested that pathological changes in the contractile elements might be of greater consequence than usually supposed. For the study of the changes in these structures the kidneys of about 100 cases of various kinds were sectioned.

The normal mucous membrane of the pelvis of the kidney contains a considerable amount of elastic tissue, which is regularly distributed in delicate fibers between the connective tissue of the mucosa, submucosa, and the muscle bundles. Elastic fibers enter, therefore, abundantly and widely into the structure of this mucous membrane. It has been found that this elastic tissue shows marked and important changes in various diseases of the kidney.

In the type of cases related above, that is, in the senile, arteriosclerotic kidney and in productive nephritis, in so far as they are uncomplicated by any diffuse inflammation of the pelvis of the kidney, the elastic tissue had become very prominent and was apparently much increased, while the connective tissue and muscular elements were atrophic and in extreme cases lost. Thus, in certain cases the elastic elements made up almost the entire bulk of the pelvic tissue. These differed, however, very markedly

from the delicate, evenly distributed fine fibers found in the normal mucous membrane. They were coarse, in places very thick and hyaline, fibrillated, frequently broken and disintegrated. The increase of elastic elements seems to be particularly marked near places where loss or fibrous contraction of kidney substance has occurred; for instance, immediately adjoining the flattened papillary portions of the kidney substance. The pictures thus obtained remind one very much of the changes occurring in arteriosclerotic arteries.

In all cases of pyelitis, whether from direct obstruction or implanted on a preëxisting hydronephrosis, or complicating a productive nephritis, the elastic tissue is destroyed, in purulent cases very rapidly, and eventually disappears entirely. This change is analogous to the behavior of elastic tissue in other inflamed organs. Non-purulent pyelitis, particularly near the papillary portion in close proximity to the kidney substance, is frequent in productive nephritis. It is difficult to determine its exact relation to the nephritic process, but it has a destructive influence on the elastic tissues of the pelvis. In this event there occurs also a gradual dilatation of calices and kidney pelvis. When this inflammatory process is localized it may be followed by elastic thickening of neighboring parts.

In a case of obstructive hydronephrosis, complicated by a pyelitis due to a cancer of the uterus, there occurred complete loss of elastic tissue. It would be interesting to investigate more thoroughly in the future the behavior of the elastic tissue in uncomplicated obstructive hydronephrosis, as well as the fate of the elastic tissue in specific inflammations of the pelvis of the kidney.

It would appear that the increase in elastic elements in the form of coarse lamellæ is probably a compensatory change incident to primary weakening and disintegration of these structures, together with progressing atrophy of the other component parts of the kidney pelvis. As in the case of arteriosclerotic arteries, it never appears to succeed in fully establishing reparation, but is prone to undergo disintegration. Thus a progressive weakening of these structures occurs, which in association with the atrophy of the fibrous and muscular parts leads to dilatation of the pelvis and stagnation of urine and true hydronephrosis.

It is not easy to determine exactly how far inflammatory conditions within the kidney parenchyma contribute toward these events. They may aid by a reduction of kidney substance, or a co-existing localized inflammatory extension within the pelvis of the kidney may be the factor. In such cases compensatory elastic thickening follows. But it has not been possible to demonstrate the formation of new elastic fibers after they have once been extensively destroyed by a general purulent pyelitis.

It does not seem that an increased urine output is of essential

consequence, as other diseases with marked polyuria, but without changes in the elastic tissue of the kidney pelvis, apparently do not lead to hydronephrosis.

Practically it remains important that an idiopathic hydronephrosis, which at times is conspiculously associated with inflammatory changes or even purulent pyelitis, is apt to occur in elderly people, and in those with contracted kidneys.

THROMBO-ANGIITIS OBLITERANS: A CLINICAL AND PATHOLOGICAL STUDY.

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Presenile spontaneous gangrene,[1] or so-called juvenile gangrene, at one time belonged to that ill-defined group of symptom complexes known as the vasomotor trophoneuroses. This group was made to embrace allied or intermediate conditions, including simple acrocyanosis[2] erythromelia, acroparesthesia[3] erythromelalgia,[4] and Raynaud's disease.[5]

From Raynaud, Mitchell, von Winiwarter, Munro, Cassirer, Strauss,[6] and, finally, Buerger, we have had various contributions on the clinical and pathological aspects of one or more of the above-named conditions. An analysis of the clinical signs and symptoms of any one of these conditions will show that they manifest themselves by a combination of one or all of three main symptom groups—vasomotor, sensory, and trophic.[7] The vasomotor include hyperemia, syncope, asphyxia; the sensory, pain, hyperesthesia, and paresthesia; the trophic, ulceration, gangrene, and dystrophies of the skin. Acryocyanosis, the simplest type, represents one symptom from the vasomotor group. Erythromelalgia includes hyperemia from the vasomotor group, and pain from the sensory. Raynaud's disease embraces all three groups; of these the vasomotor are hyperemia, syncope, and asphyxia;

[1] Leo Buerger, Thrombo-angiitis Obliterans, Amer. Jour. Med. Sci., 1908, cxxxvi, 567.
[2] Cassirer, Die Vasomotorisch tropischen Neurose, S. Karger, Berlin, 1910.
[3] Schultze, Ueber Akroparesthesie, Deutsch. Zeitsch. f. Nervenh., 1892, iii, 300.
[4] S. Weir Mitchell, Phila. Med. Times, November 23, 1872.
[5] M. Raynaud, Thèse de Paris, 1862.
[6] Arch. f. Psychiat., 1905, xxxix, 109.
[7] Barker and Sladen, Jour. Nerv. and Ment. Dis., December, 1907.

the sensory, pain, anesthesia, and paresthesia; the trophic, gangrene.[8]

Unfortunately, the pathological interpretation of these affections has not been clearly elaborated. Clinical classification, however, has advanced more rapidly and we have now numerous, nearly allied clinical conditions, satisfactorily classified, but without adequate pathological explanation. In the attempt to offer a pathological explanation for presenile spontaneous gangrene, von Winiwarter, in 1879, claimed that the terminal gangrene in many of these cases was the result of an occlusion of the lumen of the vessels by means of an obliterating endarteritis, which consisted in proliferation of the fibrous and cellular elements of the intima—endarteritis obliterans. Weiss and von Monteuffel,[9] subsequent to von Winiwarter, claimed that the disease is caused by a primary endarteritis, with the formation of a white descending thrombus, with subsequent organization and arteritis.

That *senile* gangrene is due, in most cases, to endarteritis obliterans is not questioned, but Buerger,[10] in 1908, advanced a new view, maintaining that *presenile* spontaneous gangrene was not a protean manifestation of an arteriosclerotic process, but an altogether new pathological entity, depending upon the primary formation of *obturating thrombi* in the arteries and veins, and to which he gave the name thrombo-angiitis obliterans.[11] He showed that the red thrombus is the precursor of the condition; that the process does *not* extend from above but from below upward; and that the lesion may occur in vessels devoid of endarteritis.

According to Buerger,[12] presenile spontaneous gangrene is a distinct clinical and pathological entity, characterized by thrombotic occlusion of arteries alone, or of arteries and veins, giving subjective manifestations, chief among which are pain and the peculiar symptom of intermittent claudication, and presenting objective phenomena, the most important of which are redness in the dependent position of the limb (erythromelia), marked blanching in the elevated position, evidence of arterial occlusion in the form of pulseless vessels (popliteal, anterior and posterior tibial, dorsalis pedis, etc.), trophic disturbances of moderate extent and of even grave consequence, often terminating in gangrene of one or both lower extremities. Clinically, thrombo-angiitis obliterans may show many variations from a set form, and this accounts for the fact that the true condition is so frequently over-

[8] Barker and Sladen, loc. cit.

[9] Cited by Buerger and Brooks, Jour. Med. Research, September, 1911, vol. xxv, No. 247.

[10] Loc. cit.

[11] Quite recently Ch. Baumler describes this condition under the caption Arteritis Thrombotica, v. Benzoldt and Stintzing, Med. and Therapie. (Personal communication from Dr. Buerger.)

[12] Amer. Jour. Med. Sci., January, 1910.

looked. Brooks[13] thinks that the vascular changes alone do not explain all the manifestations, but that the condition is also trophic in origin, and his histological studies showed distinct interstitial and parenchymatous neuritis and atrophic changes in the voluntary muscles, apparently secondary to the neuritis.

The gross process may be said to embrace distinct morbid processes. (1) An obliteration of the lumen of the large arteries and veins by means of an obturating thrombus, which later becomes vascularized and organized by growing in of "capillary buds" from the media and adventitia with subsequent canalization of the thrombotic tissue. (2) A periarteritis and periphlebitis, with a marked agglutinative process, due to fibrous tissue proliferation in and about the adventitia, and which binds arteries, veins, and nerves together into one conglomerate cord. In some cases, the agglutination is so dense and firm as to render dissection into the component elements almost impossible. (3) An associated or coincidental arteriosclerosis of varying degree.

In a typical case (quoted from Buerger)[14] "the vessel is seen to be filled with a grayish or yellowish mass that can be distinctly differentiated from the annular wall of the vessel, and that appears to be pierced at one point (more rarely at a number of points) by an extremely fine opening through which a minute drop of blood can be squeezed. Such obturating tissue is firm in consistency and does not at all resemble the crescentic or semilunar occluding masses typical of arteriosclerosis. The vessel itself is usually contracted, so that its wall appears somewhat thickened." The vessels most often affected are those of medium caliber—the small distal arterioles are rarely if ever involved, and the tendency is for the thrombosis to extend up the leg rather than down. If a sufficient number of sections are made, the process may be followed from the fresh, red, recent thrombus, with a cone-shaped extremity, projecting into the lumen of an apparently normal vessel, to the old gray, yellow organized clot. Some arteries may be entirely free from the disease (in our case the peroneal artery was absolutely intact), while other vessels (anterior tibial, posterior tibial, dorsalis pedis, etc.) may show morbid changes of varying degrees of intensity. Buerger, therefore, concludes that the apparently normal condition of the vessel above and below the occluding masses, and the transition into the thrombosed areas speak for a thrombo-angiitis and thrombophlebitis instead of a proliferative obliterative process from the intima of the arteries and veins.

Histological examinations of the stained sections show a considerable amount of organized blood clot, occluding the lumen and often associated with certain characteristic changes in the media. The whole picture gives the impression of an extensive

[13] Jour. Med. Research, September, 1911, vol. xxv, No. 247. [14] Loc. cit.

intimal and subintimal proliferation, hence the original designation endarteritis obliterans. Further study, according to Buerger, by means of special elastic tissue stains, shows that there is no intimal hyperplasia, but that the new tissue arises from organization at the periphery of an obliterating thrombus; in arteriosclerosis there is a large amount of elastic tissue parallel to the internal elastic tissue membrane and extending into and being incorporated with the characteristic sclerotic plaques. In the process under discussion, there is no noteworthy increase in elastic tissue, and such newly formed tissue as is observed can readily be seen to arise by organization at the periphery of a thrombus.

Thrombo-angiitis obliterans usually manifests itself by well-defined clinical signs and symptoms. The course of the disease, however, is variable, but is well illustrated by the following case:[15]

S. K. (Case No. 15,241), male, aged forty-nine years; a Hebrew, born in Poland; has lived in New York City for the last thirty years, during the last seventeen of which he has been employed as a street cleaner. The patient entered the hospital on November 18, 1910, complaining of "pain in the feet." Interesting features in the family history are fatal diabetes mellitus in an uncle and a cousin. The patient states that he has enjoyed excellent health up to the present illness. Venereal infection is denied and there is nothing in his personal history to suggest a syphilitic infection. For the last twenty years the patient has indulged in beer and whisky rather freely. For fifteen years he was in the habit of drinking three or four glasses of whisky daily, and for the last three years has been a considerable user of beer. Throughout his life the patient has smoked considerably, averaging twenty cigarettes per day. About two years ago he became impotent, which condition has persisted up to the date of his admission to the hospital.

The present illness began eight months ago, when the patient commenced to experience a "cold feeling" or a sense of numbness in the toes of the right foot in cold weather. This numbness was always associated with low temperatures and was not induced by inclemency of the weather. Occasionally, the left foot would be similarly affected, while at other times, both feet would be affected simultaneously. This feeling of numbness would come on about eight o'clock in the morning; the toes would appear blanched and were "apparently dead." After rubbing the toes or walking for a few minutes, the blanched, cadaveric appearance would be replaced by a dark red suffusion, quickly becoming livid or cyanotic. There were sporadic attacks of pain—cramp-like in character—in the calf of the leg, which would interfere,

[15] We are indebted to Professor Edward Quintard for the privilege of reporting this case, from the medical wards of the New York Post-Graduate Medical School and Hospital.

temporarily, with locomotion. This condition, of alternating ischemia and erythromelia, persisted, with slight if any change, for about three months, when the patient began to experience "indefinite pains" in the sole of the right foot, associated with "drawing sensations" along the upper and inner part of the leg. Elevation of the leg from the pendant position to beyond the horizontal would elicit excruciating pain, while the toes would become extremely pale and bloodless. A short time after the onset of the above pain, the patient became "short of breath" upon exertion. For his dyspnea he visited various dispensaries and was treated for "heart disease" for a number of weeks, with a resulting gain in weight and strength.

The above symptoms persisted unabated up to three weeks before his admission, when the pain became very greatly exaggerated and was compared with the "sticking of pins" in the toes, or like "blowing steam over the foot," and was so severe as to prevent walking. Coincidently, an eczematous rash appeared over the arms, legs, and abdomen, characterized by an intense pruritus.

Physical Examination: Temperature, 98.6°; respiration, 16; pulse, 100; weight, 122 pounds. The patient is a fairly well-nourished man, aged about fifty years, and does not look ill. The skin shows a diffuse, scaly, red, maculopapular eruption, with numerous scratch marks, suggesting eczema. There are many dilated venules over the cheeks and nose. The lips, ears, and finger tips are slightly cyanotic. The pupils are round, equal, and react to light and accommodation. A well-marked venous pulsation is to be seen in both external jugulars. The superficial glands show a moderate degree of adenopathy. Examination of the lungs reveals a moderate emphysema with slight relative dulness over the right apex. Expiration is prolonged, of low pitch, and accompanied by "wheezing rales." The heart is normal in size and outline; there are no murmurs or thrills. The first sound, at the apex, is somewhat rough, while the second sound, at the base, is only slightly accentuated. The blood pressure determination shows systolic, 120 mg. of Hg; diastolic, 75 mg. of Hg. The abdomen, spine, rectum, and external genitalia are negative. The reflexes are somewhat sluggish, but react equally. All the toes of the right foot and to a lesser extent the left foot are markedly livid when held in the pendant position. In the horizontal position the color is lessened to a pink, which spreads over the dorsum and sole of the foot. At an elevation of 15 degrees, "the angle of circulatory sufficiency," the foot becomes normal in appearance, while at 35 degrees of elevation the foot becomes markedly ischemic with the simultaneous development of excruciating pain. There are no blebs or ulcerated areas. The femoral artery pulsates, but no pulsation can be determined in the popliteal, dorsalis pedis, or posterior tibial arteries. The toes are extremely

sensitive to pressure; movement causes great pain. Along the inner and upper portion of the tibia are a few irregular, tender nodosities, not attached to the overlying skin and apparently belonging to the internal saphenous vein.

Blood examination: Hemoglobin, 70 per cent.; erythrocytes, 3,500,000; leukocytes, 10,000. Differential count: Polynuclears, 71 per cent.; large lymphocytes, 10 per cent.; small lymphocytes, 19 per cent.; eosinophiles, 4 per cent. Repeated complement fixation tests, both by the Wassermann and Noguchi methods, were negative. The coagulation time was normal, with the Russell-Brodie apparatus.

X-ray examination of both extremities showed no bony abnormalities.

Urinalysis. The average daily excretion amounted to about 800 c.c. The urine was acid, of specific gravity, 1025; showed no albumin and no sugar. Microscopically, there were found a few hyaline casts, a few disintegrated pus cells, no erythrocytes and no crystalline matter.

Subsequent course: From the time of admittance on November 18, 1910, until December 6, nineteen days in all, the patient presented no distinct signs of any trophic disturbance. On December 7 there appeared upon the under surface of the second toe of the right foot a small purple area, surrounded by a zone of inflammation, which marked the beginning of a definite gangrenous process. Within a few days the entire distal phalanx progressed to complete gangrene. Coincidently, a small gangrenous area appeared along the outer border of the little toe of the same foot. This latter process was very slight and quickly subsided. However, on December 23, the two distal phalanges of the second toe were completely gangrenous with a moist, ill-defined line of demarcation. Within the succeeding month, contact ulcers began to appear on the adjacent borders of the first and second toes at the points of apposition with the gangrenous second toe. On February 9, or eighty-three days from the time of admittance, areas of gangrene began to appear over all the remaining toes. A large hemorrhagic bleb extended from the base of the toes, well up over the dorsum of the foot and passed gradually into a miliary, vesicopustular eruption with marked intervening lividity. During this time there were no changes taking place in the left foot.

Treatment consisted of hot air baths twice a day, to both legs, at a temperature of 140° to 180° F., with local applications of the official belladonna ointment, and codeine in grain doses, when necessary, for pain. There was some relief of pain, but the gangrenous process progressed. Amputation was recommended and readily assented to by the patient. On February 13, 1911, the right leg was amputated above the knee by Dr. Samuel Lloyd. The wound healed by primary union and the patient was discharged on March 3, 1911, apparently well.

Pathological Report. A very careful anatomical dissection of the vessels of the amputated limb showed extensive thrombotic involvement of all the large arteries and veins. In the popliteal artery the process commenced at about the upper level of the condyles of the femur, and from this point to the bifurcation there was a typical thrombotic occlusion of the lumen of the vessel. At the proximal end was found a recent, bright, red thrombus with conical extremity which passed gradually into a yellow material not unlike bone marrow, but of firmer consistency. In a few places the continuity of the occluding thrombus was interrupted by the appearance of clear spaces, bounded by apparently normal intimal walls. Near the point of bifurcation the material was gray and showed the beginning of canalization of the thrombus by two pin-point channels, through which minute drops of blood could be squeezed. The anterior and posterior tibial arteries showed similar thrombotic changes, in varying degrees of intensity, with organization and canalization and the production of intermediate clear spaces. Surrounding the posterior, and, to a lesser extent, the anterior tibial artery was a marked agglutinative process, the evidence of an extensive periarteritis. The artery, nerves, and veins were bound together into a dense conglomerate cord. In striking contrast to the above, was the peroneal artery, which throughout its course was macroscopically intact, without any sign of intimal or occlusive changes. The dorsalis pedis showed the general type of thrombus formation and did not differ from the above picture, except in the apparent lessened intensity of the process. The smaller arteries, such as the dorsalis hallucis, calcaneus, and plantar, showed very slight, if any, involvement, while the finer arterioles were apparently perfectly normal. Associated with the arterial condition was a striking coincident thrombophlebitis. Below the knee both the internal and external saphenous veins showed nodules of thrombotic origin. Surrounding the veins, as in the case of the arteries, were agglutinative changes suggesting a moderate periphlebitis.

The history of this case, from numbness and ischemia to gangrene, embraces roughly only eight months. It is interesting to note the evidence of an associated thrombophlebitis of the superficial veins.[16] The clinical signs of superficial venous involvement were the few nodules along the course of the internal saphenous vein. The early symptoms of numbness and ischemia pointed to the beginning of an acutely progressive thrombo-angiitis obliterans, which later became more apparent by the appearance of trophic changes, culminating in gangrene.

After leaving the hospital the patient returned from time to time to the dispensary, complaining of pain and cramps in the left

[16] Buerger, Jour. Amer. Med. Assoc., lii, 1319; International Clinics, vol. iii, ser. 19.

leg, more particularly in the left foot. About July 1, 1911, a dark blue discoloration appeared over the entire dorsum of the left foot, and the pain became so severe that the patient entered the hospital on July 12, 1911, and a week later was transferred to the surgical division. The patient insisted on operation as the only relief from the excruciating pain. On July 24 the left leg was amputated just above the knee by Dr. Peterson. The patient reacted well and his condition was satisfactory until the 29th, when, suddenly, he had a severe attack of vomiting and pain, which persisted unabated for the five succeeding days. Physical, gastric, and blood examinations were all negative, and on August 5, 1911, the patient died, apparently from exhaustion. Thrombotic occlusion of mesenteric vessels was thought possible, but, unfortunately, autopsy was refused.

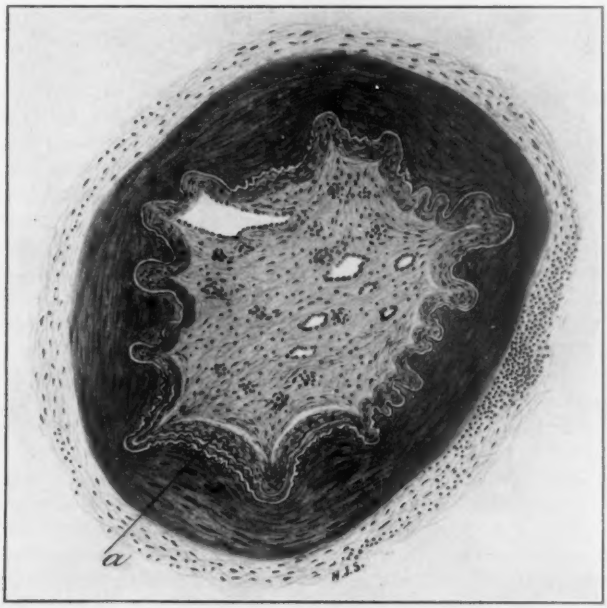
Anatomical dissection of the amputated limb showed changes identical with those found in the right leg. The morbid process had not extended to such a severe grade of arterial occlusion, nor were the evidences of venous involvement so marked, although there was a moderate periphlebitis about the internal saphenous vein.

Conclusion. The type of gangrene represented by this case occurs in non-luetic young people,[17] invariably men, with a low blood pressure, and before the age of marked angiosclerotic changes, hence, the name presenile or juvenile gangrene. The contention that this condition presents a fairly distinct clinical and pathological entity seems justifiable. Although it is true, as Huchard[18] has shown, that we may have a marked arteriosclerosis with a low blood pressure, it seems extremely improbable that there is any marked sclerosis present in these cases. Histological study of the nerves and muscles from the affected areas showed neuritis and atrophy respectively. Careful study of specially prepared sections showed occasional proliferation of the elastic tissue lamina, characteristic of arteriosclerosis. There were no plaques nor crescentic lamellæ decreasing the caliber of the arteries such as we usually meet with in well-marked cases of angiosclerosis.

We were able to establish clearly, however, a proliferative process in the intima and to a slight extent in the subintimal tissue, leading to a considerable increase in the endothelial cells which encroached upon, and became part of, the organization and the periphery of the thrombus. In addition, we could clearly determine that there was a partial reduplication of the internal elastic tissue membrane which strongly suggested a pure arteriosclerotic process (see illustration). Buerger contends that such newly formed tissue is purely a coincident endarteritis and that the thrombus is primary

[17] Leo Buerger and David J. Kaliski, Med. Rec., New York, October 15, 1910.
[18] Monde Méd., October, 1909.

and the endarteritis secondary. However, if we believe that thrombosis does not occur in a normal vessel,[19] and that an injured intima is necessary for thrombus formation, we have a more probable explanation for the obturating thrombus in a primary intimal change—arteriosclerotic—with consecutive thrombosis and organization of the thrombus. We found no evidence to support the idea of a gradually organizing mural thrombosis with eventual occlusion.



Thrombo-angiitis obliterans: Drawing from a section of the dorsalis pedis artery, showing occlusion of the lumen by an obturating thrombus in which the process of organization and canalization are well shown. Inferiorly (at *a*) there is well-defined evidence of proliferation of the endothelial cells and subintimal cells with partial reduplication of the internal elastic membrane.

That the actual occlusion is due to thrombosis there is hardly any doubt, but from our study we are of opinion that the question whether the thrombosis is the primary agent, whether the condition is a combined arteriosclerosis and thrombosis, or whether the condition is primarily due to neuritis is still an open one.

[19] H. T. Brooks, General and Special Pathology. In press.

THE EFFECT OF CAFFEIN ON NITROGENOUS EXCRETION AND PARTITION.[1]

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The effect of caffein on nitrogenous excretion has been a subject of interest to investigators for some sixty years. Lehmann,[2] in 1853, found that under the influence of caffein there was a diminution in the excretion of urea amounting to 12 to 20 per cent. This was confirmed at first by other physiological chemists and supported, if it did not give rise to, the hypothesis that caffein lessens tissue waste. This specious phrase seems to have implied that caffein so increased the efficiency of the metabolic processes that a great economy in the consumption of nitrogenous matter was effected.

Unfortunately for this supposition subsequent work for the most part failed to confirm Lehmann's results; thus Hoppe,[3] in carefully controlled experiments on dogs, found that caffein had no effect on the excretion of urea; Roux,[4] in human beings, unaccustomed to the use of coffee, found a temporary increase in the amount of urea and other solid materials, while Le Blond[5] obtained results corresponding with those of Hoppe. Reichert[6] made use of the calorimetric method which he thought showed, beyond possible doubt, that caffein increased heat production and, as a corollary, increased destructive tissue metamorphosis. Dr. H. C. Wood,[7] while agreeing that it does not "appear probable that caffein has any distinct specific influence upon protoplasmic nutrition" has pointed out that Reichert's results are not conclusive as regards nitrogenous metabolism.

Our work was not undertaken with any reference to this old controversy, but will be found (at least for small doses), to confirm by modern methods the position of those who denied any specific effect of caffein in economizing nitrogen.

Before describing our experiments we will refer to two "Dissertations," which have an indirect bearing on the subject of the

[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, October 23, 1911.

[2] Quoted by Reichert, q. v.

[3] Deutsch. Klinik, 1857, vol. ix.

[4] Arch. de Physiol. Norm. et Path., 1874, p. 578.

[5] Paris Thesis, 1883.

[6] New York Med. Jour., April 26, 1890.

[7] Treatise on Therapeutics, 1894.

present paper, one by Schneider[8] and the other by Rost,[9] and both concerned with the fate of caffein in the animal body and its mode of elimination. The former found that it was largely decomposed in the organism, though it might appear in the urine if the dose were very large or the diuresis profuse. The latter found that after the administration of caffein as much as one-fourth of the amount ingested appeared again in the urine. It will be seen that our tables point to the latter conclusion as the correct one.

Our peculiar purpose was to observe the effect of various diuretics on the elimination of the total nitrogen, and particularly to investigate any deviation from the normal in the relative amounts eliminated as urea, uric acid, ammonia, creatine, purin bases, etc. In collaboration with Dr. Riesman we had previously studied the action of theophyllin from the same point of view, both in healthy persons and in nephritics.[10] In the 2 normal cases reported here we used the greatest care in securing uniform experimental conditions and in employing the most accurate methods of analysis.

The Folin diet was employed largely because it gave us the advantage of comparing our figures with the results of his "Complete Analysis of Thirty 'Normal' Urines" (five persons[11]).

The diet consisted of whole milk, 500 c.c.; "Horlick's malted milk," 200 grams; cream (18 to 22 per cent.), 300 c.c.; sugar, 20 grams; eggs (white and yolk), 450 grams; sodium chloride, 6 grams; water to make the whole up to 2 liters. Extra water to drink, 900 c.c. This diet represents 119 grams protein, 148 grams fat, and 225 grams carbohydrates, and yields 2800 (2786) calories, or enough for a man of 70 kg. (Voit).

The subjects of the experiment were fellow laboratory workers who had an intelligent interest in securing accuracy. In preparing the diet, certified milk was employed to insure as uniform a composition as possible. The methods of analysis were described in a previous article, in which one of us[12] collaborated, and may be enumerated as follows: Total nitrogen, Kjeldahl's method; ammonia nitrogen, Folin's method; urea, Folin's method; uric acid, Folin-Shaffer method; creatinin, Folin's colorimetric method; purin bases, combined Salkowski and Arnstein method (Welker); undetermined substances, by subtraction. Folin did not estimate the purin substances, and in his tables they are, therefore, included under the last-named heading.

The tables showing our results require little comment.

[8] Dorpat, 1884.
[9] Leipsig, 1895.
[10] Philadelphia Gen. Hosp. Rep., 1911.
[11] Folin, Amer. Jour. Phys., vol. xiii, p. 45.
[12] Dittman and Welker, New York Med. Jour., May 15, 22, 29, and June 5, 1909.

TABLE I.—Case "W." Daily Records

Experimental day.	Volume c.c.	Specific gravity.	Reaction to litmus.	Ammonia nitrogen grams.	Creatinin grams.	Caffein grams.	Remarks.
PRELIMINARY PERIOD FOR DIET ADJUSTMENT.							
1							
2							
3							
NORMAL PERIOD.							
4	1200	1.025	Acid	0.6283	1.4840	0.00	
5	1895	1.020	Acid	0.6208	1.6684	0.00	
6	1270	1.024	Acid	0.6863	1.6073	0.00	
EXPERIMENTAL PERIOD.							
7	1108	1.029	Acid	0.7073	1.6318	0.390	Warm weather.
8	875	1.032	Acid	0.6370	1.6676	0.390	Very warm weather.
9	1070	1.030	Acid	0.6501	1.5205	0.390	

TABLE II—Case "W."

Period.	Experimental days.	Total nitrogen.	Nitrogen of ammonia	Nitrogen of urea.	Nitrogen of uric acid.	Nitrogen of purin base.	Nitrogen of creatinin.	Nitrogen of undetermined bodies.
PERIOD TOTALS.								
I	4th to 6th	45.7710	1.9354	39.6916	0.4785	0.0104	1.7694	1.8857
II	7th to 9th, caffein .	46.1960	1.9945	40.1325	0.3497	0.2330	1.7915	1.6948
DAILY AVERAGES.								
I	4th to 6th	15.2570	0.6451	13.2305	0.1595	0.0035	0.5898	0.6286
II	7th to 9th, caffein .	15.3987	0.6648	13.3775	0.1166	0.0777	0.5972	0.5649
PERCENTAGES ON THE BASIS OF TOTAL NITROGEN.								
I	4th to 6th	....	4.23	86.72	1.05	0.02	3.87	4.12
II	7th to 9th, caffein .	....	4.32	86.86	0.76	0.50	3.87	3.67

TABLE III.—Folin's Results on the Diet Used in These Experiments (From the Analysis of 30 Normal Urines).

	Total nitrogen.	Nitrogen of ammonia.	Nitrogen of urea.	Nitrogen of uric acid.	Nitrogen of creatinin.	Nitrogen of undetermined bodies.
AVERAGE DAILY EXCRETION.						
High limits	18.2	0.85	16.2	0.15	0.66	0.85
Low limits	14.8	0.55	12.8	0.08	0.50	0.41
Average	16.0	0.70	13.9	0.12	0.58	0.60
PERCENTAGE ON BASIS OF TOTAL NITROGEN (5 CASES).						
High limits	....	5.0	89.4	1.00	4.50	5.30
Low limits	....	3.3	86.2	0.60	3.20	2.70
Average	....	4.3	87.50	0.80	3.60	3.75

TABLE IV.—Case "M." Daily Records.

Experimental days.	Volume c.c.	Specific gravity.	Reaction to litmus.	Ammonia nitrogen, grams.	Creatinin, grams.	Caffein, grams.	Remarks.
PRELIMINARY PERIOD FOR DIET ADJUSTMENT.							
1							
2							
3							
NORMAL PERIOD.							
4	1770	1.019	Acid	0.6839	1.7921	0.00	
5	1492	1.022	Acid	0.8088	1.6790	0.00	
6	1480	1.019	Acid	0.6879	1.7630	0.00	
EXPERIMENTAL PERIOD.							
7	1190	1.024	Acid	0.5998	1.5806	0.390	
8	1770	1.019	Acid	0.6046	1.5252	0.390	
9	2368	1.017	Acid	0.6365	1.8268	0.390	

TABLE V.—Case "M."

Period.	Experimental days.	Total nitrogen.	Nitrogen of ammonia	Nitrogen of urea.	Nitrogen of uric acid.	Nitrogen of purin base.	Nitrogen of creatinin.	Nitrogen of undetermined bodies.
PERIOD TOTALS.								
I	4th to 6th, normal .	50.549	2.1806	42.2994	0.4434	0.0709	1.9457	3.6090
II	7th to 9th, caffein .	49.828	1.8409	44.0281	0.3872	0.2489	1.8336	1.4893
DAILY AVERAGES.								
I	4th to 6th, normal .	16.8497	0.7269	14.0998	0.1478	0.0236	0.6386	1.2030
II	7th to 9th, caffein .	16.6093	0.6136	14.6760	0.1291	0.0830	0.6112	0.3964
PERCENTAGES ON BASIS OF TOTAL NITROGEN.								
I	4th to 6th, normal .	....	4.32	83.68	0.88	0.14	3.85	7.14
II	7th to 9th, caffein .	....	3.70	88.36	0.78	0.50	3.68	2.99

Table I presents the "daily records" of Case "W." During the "Preliminary Period" of three days the diet was strictly adhered to, but no specimens were saved. During the normal and experimental periods daily estimations of ammonia nitrogen and creatine were made with the fresh specimen. The other estimations were made in combined "aliquot" samples at the end of each period. During the "Experimental" period the weather was very hot, and this, by producing diaphoresis, prevented any diuresis that might otherwise have occurred.

Table II. The first part of this table shows the total nitrogen for each period and the fractional portions for each constituent; in the case of ammonia and creatinin calculated from the previous table. In the second part these figures are reduced to daily averages In the third part they are shown as percentages on the basis of the total nitrogen. Comparison with Folin's results in Table III fails to show the slightest deviation from the normal. The purin base nitrogen increased from 3.5 mg. to 77.7 mg., mani-

festly due to the ingested caffein which represents about 113 mg. of nitrogen.

Tables IV and V belong to Case "M" and are similarly constructed. The daily records show that there was a slight diuresis during the caffein period as a whole, probably not significant. The final tabulation in Table V again shows nearly normal figures. In the normal period there seems to have been some disturbance in metabolism manifested by a diminution in the percentage of urea and a corresponding increase in the undetermined substances. The normal relations were restored in the caffein period, but it is doubtful if we can attribute this to the drug. The purin nitrogen is here also increased (from 23 to 83 mg.), again corresponding to about half of the caffein ingested.

CONCLUSIONS: 1. In the amount given, corresponding to a small daily medicinal dose or to three ordinary cups of coffee, caffein produced slight if any diuresis.

2. The purin nitrogen was increased. This was due in all probability to the elimination of the caffein.

3. The total nitrogen remained unaltered and no abnormalities in the distribution of the nitrogen were observed, with the exception of the increase in the quantity of the purin nitrogen. Caffein in the doses given would therefore appear to exert no disturbing influence on nitrogen metabolism in man.

4. There was no evidence that caffein lessened tissue waste, in the sense of the older writers.

5. Clinical experience teaches us that large therapeutic doses of caffein produce diuresis. The effect of such large doses on nitrogen metabolism cannot be accurately predicted, but it would seem probable that no marked disturbance would result.

The work described in this paper was performed at the suggestion and under the direction of Prof. John Marshall. We desire to express here our appreciation of his kindly interest and suggestions.

REMARKS ON CARDIOSPASM, WITH SPECIAL REFERENCE TO TREATMENT AND THE USE OF THE ESOPHAGOSCOPE FOR EXAMINATION, BASED ON A STUDY OF SEVENTEEN CASES.

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BY the "cardia" anatomists understand the junction of the esophagus with the stomach, indicated by a rough zigzag line where the pale pink mucous membrane of the esophagus unites with the deeper red mucosa of the stomach.

To the cardia has been ascribed the physiological closure of the esophagus toward the stomach, but recent experiments of Schreiber have shown that the "epicardia" is the part which effects this closure. By epicardia is understood the part of the esophagus from the cardia to about the hiatus esophageus, 4 to 5 cm. long, and comprising the abdominal and the diaphragmatic parts.

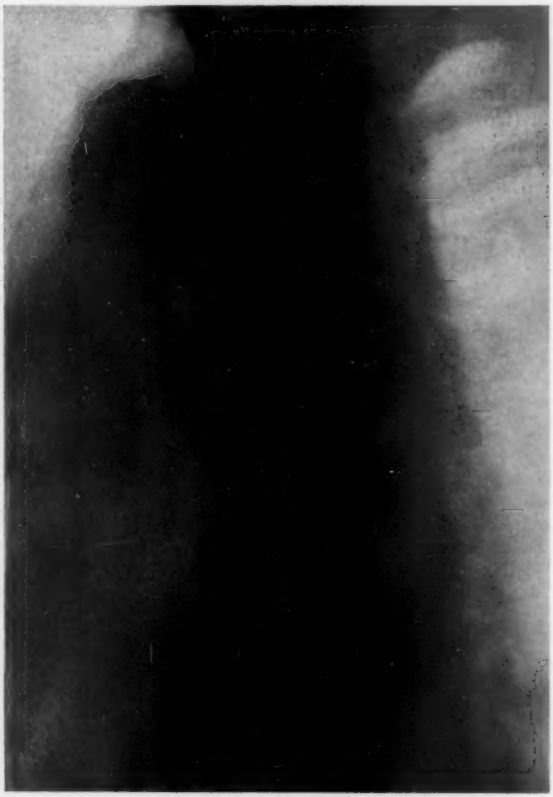

FIG. 1.—*X*-ray picture, showing pear-shaped dilatation of the esophagus from Case IV.

The name cardiospasm, which was given by Mikulicz to the spastic closure of the lower end of the esophagus, naturally conveys the idea that the anatomical cardia is the only part affected, but I am convinced that this is not always so, because in a number of cases of so-called cardiospasm, which I have examined through the esophagoscope, I have found the epicardia to be involved in the spastic contraction. The name cardiospasm, therefore, seems

somewhat inadequate. I think that it is of importance to keep this in mind in the study of the pathological conditions in these cases, because otherwise one might be led to erroneous conclusions as to the nature of the obstruction encountered unless the esophagoscope is used in the examination. Thus, when the epicardia is spastically closed and the esophagus is dilated immediately above

FIG. 2.—*X*-ray picture of a dilated esophagus, the largest diameter of which is in the upper thoracic part.

the diaphragm forming a pouch against the bottom of which the examining sound strikes, tumor and twisting or angulation of the canal may be imagined to be the obstructive cause. If the epicardia was open the sound would more readily become engaged and easily overcome any resistance of the cardia.

I know of a number of cases in which the obstruction was thought

to be caused by a newgrowth, in which the esophagoscopic examination proved it to be due to cardiospasm and *vice versa*.

Strümpel, in 1881, reported a case in which he had made a diagnosis of dilatation of the esophagus due to angulation of the lower end of the organ. In this case Weigert made the postmortem and found no angulation nor other obstruction; it was an ordinary case of cardiospasm with dilatation.

A diagnosis of angulation *intra vitam* cannot well be accepted unless proved by esophagoscopic examination.

FIG. 3.—Specimen of an enormously dilated esophagus

The shape of the dilated esophagus varies in the different cases. The majority of cases that have come under my observation have had the largest diameter in the lower third, like Fig. 1, which I should call pear-shaped. Case II had the largest diameter in the upper thoracic part, which is unusual. (See Fig. 2.) Spindle-shaped, cylindrical, and bottle-shaped forms have been described.

Fig. 3 shows a specimen of an enormously dilated esophagus, which I had the opportunity to examine in the Pathological Institute in Vienna through the courtesy of Professors Weichselbaum and Gohn. The capacity of such a dilated esophagus may be

as high as one and one-half quarts. The mucous membrane is frequently the seat of chronic catarrh, and appears through the esophagoscope white and edematous, and at times shows inflamed red patches or streaks. Ulcers or scars therefrom may be present. The entire wall of the esophagus may be hypertrophic, the different layers participating in this, but particularly so the circular muscular layer. More rarely the esophageal wall is atrophic and appears to be thinner than usual. The epicardia-cardia is almost always found normal. The esophageal wall may be thinner in parts. The right wall is particularly prone to sag down on the diaphragm and form a pouch.

ETIOLOGY. Two groups of diffuse dilatation of the esophagus without anatomical obstruction can be recognized. In one, spasm of the cardia is primary and the dilatation of the esophagus secondary. The cause of the spasm may be disturbance in some neighboring organ or irritation along the pneumogastric nerve. A neurotic temperament plays an important part in some cases. In the other group atony of the esophageal wall is primary and the cardiospasm is secondary.

Kraus has described a case of a greatly dilated esophagus with cardiospasm, in which at postmortem changes in the pneumogastric nerve were demonstrated. In the left vagus less than one-half of the normal nerve bundles appeared to be intact. Any pathological process in the esophagus may give rise to cardiospasm. Cardiospasm secondary to a newgrowth, ulcers, etc., will not be discussed here.

Sex. In my series of cases 10 were men and 7 women.

Age. Cases of cardiospasm have been reported in early childhood. In one of my patients it started at the age of fourteen years. The oldest person that I have treated for cardiospasm was aged eighty-four years.

PROGNOSIS. Some cases of primary cardiospasm with diffuse dilatation of the esophagus seem to remain well after stretching. Others, apparently similar cases, will suffer a relapse. The etiology in each case must be taken into consideration in giving a prognosis. The treatment of cardiospasm by stretching has been in vogue only a few years and sufficient time has not elapsed to determine what percentage of cases will remain permanently cured. One writer recently made the statement that he had not seen any case of this kind that was not completely cured by dilating the cardia. Some time ago I had under observation a patient who had previously been treated for cardiospasm by this observer. The patient had recurrence of the trouble and was worse off than ever.

SYMPTOMS AND DIAGNOSIS. The initial symptoms vary somewhat. A sensation of choking while eating, immediately followed by regurgitation of food is the earlier manifestation in some patients. In others, a sensation of the food sticking behind the upper part of the

sternum and slowly passing down may be noticed now and then for months before a choking spell during meal with regurgitation of food comes on. One patient had severe burning in the throat, relieved by drinking cold water, for many months before regurgitation began. Later, these patients regurgitate some of the food and large quantities of slime at intervals after eating, and they will take large draughts of water with their meals, in order to force the food into the stomach. Sometimes there is a night cough due to aspiration of the esophageal contents during sleep. There may be considerable loss of weight.

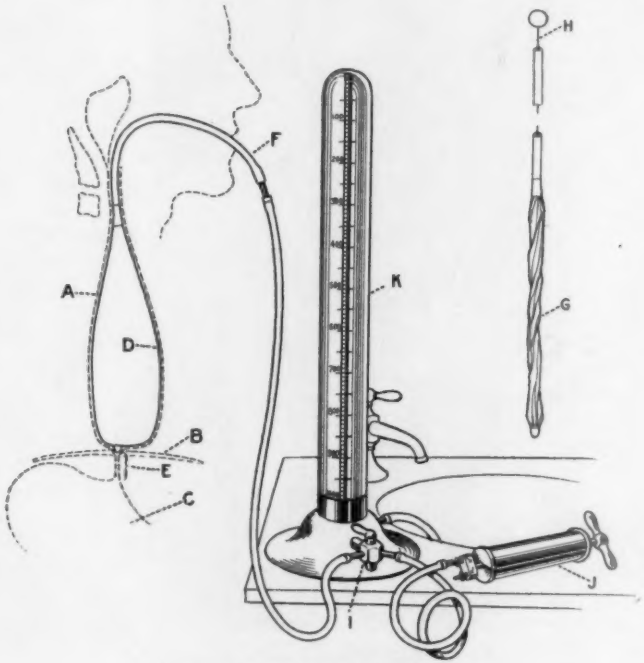

FIG. 4.—Author's esophagometer.

Pain in the chest or in the epigastrium is experienced by some. In one of my patients severe pain in the chest radiating to the back and both sides of the neck came on in paroxysms.

After a careful general examination a stomach tube stiffened by a wire stylet is introduced into the esophagus in order to measure the distance from the incisor teeth to the obstruction, and also to determine the resistance of the spastic epicardia-cardia. The stylet is then removed, and if there is any contents present in the esophagus it can be drawn off through the tube. The use of the tube

with the stylet saves the extra introduction of a sound. The next step is to measure the capacity of the dilated organ, which can be quickly accomplished by the use of my esophagometer (Fig. 4). This is done by introducing a large thin rubber bag (*G* and *D*), attached to a stomach tube, into the esophagus by the aid of a wire stylet (*H*), and then distending the bag with air (as suggested by Strauss), which is then drawn off and measured. By first turning the stopcock handle (*I*) toward the air-pump attachment and exhausting the air in the glass cylinder (*K*), the water from the bowl should fill the cylinder to the top of the inner glass tube. Then turning the handle toward the rubber bag attachment, the air pump is reversed and air is slowly pumped into the rubber bag in the patient's esophagus until the patient complains of pressure in the chest. If the handle is then turned toward the glass cylinder, the air in the rubber bag will be sucked into the cylinder. The number of cubic centimeters of air that the dilated organ will hold can then be read off on the scale. I first described this apparatus in the *St. Paul Medical Journal*, April, 1908, but have later modified it somewhat. In my work this method has been used for the purpose of estimating the size of the dilatation only, and not for making a differential diagnosis between a low-seated diverticulum and dilatation of the esophagus, as advocated by Strauss, because the two conditions may co-exist, hence the method might mislead. If desired, an *x*-ray picture may now be taken after filling the above-mentioned rubber bag with 10 to 20 per cent. subnitrate of bismuth suspended in some thick fluid. I use strained oatmeal gruel. The picture is then taken from right to left (Fechterstellung) or anteroposteriorly.

The most important step in the examination comes last, namely, the esophagoscopic examination of the organ. By the aid of the esophagoscope the distance from the incisor teeth to the obstruction can be measured, the capacity of the esophagus roughly estimated, the shape of the dilatation observed, and the presence of a diverticulum excluded.

As a matter of fact, the esophagoscope can supplant all the other above mentioned means of diagnosis. In addition, the condition of the wall of the esophagus can be studied through this instrument. The necessity of esophagoscopy in every case will at once be apparent when we know that the esophageal mucosa may be the seat of various lesions such as ulcer, newgrowth, acute or chronic catarrh, etc.; or the wall may be in a state of atony or spasm. The irritation from such lesions may cause recurrence of the spasm after the stretching, and the knowledge of their presence is, therefore, essential. Furthermore, stretching of the epicardia-cardia without first having excluded pathological lesions by inspection through the esophagoscope might prove disastrous.

As a rule, the sound will pass the spastic epicardia-cardia on

gentle, steady pressure. In 2 of my cases, however, the epicardia was so firmly closed by the sapsm that it did not admit the sound. The esophagoscope was introduced and the probe applied under the guidance of the eye, with the same result. I then rubbed the epicardia with a 10 per cent. cocaine solution on the cotton applicator, after which the epicardia-cardia opened and could be inspected. *In no case of cardiospasm is the epicardia-cardia impermeable.* Sounds of different pattern give very little dependable information in these cases; the esophagoscope is the only instrument by which a positive diagnosis can be made.

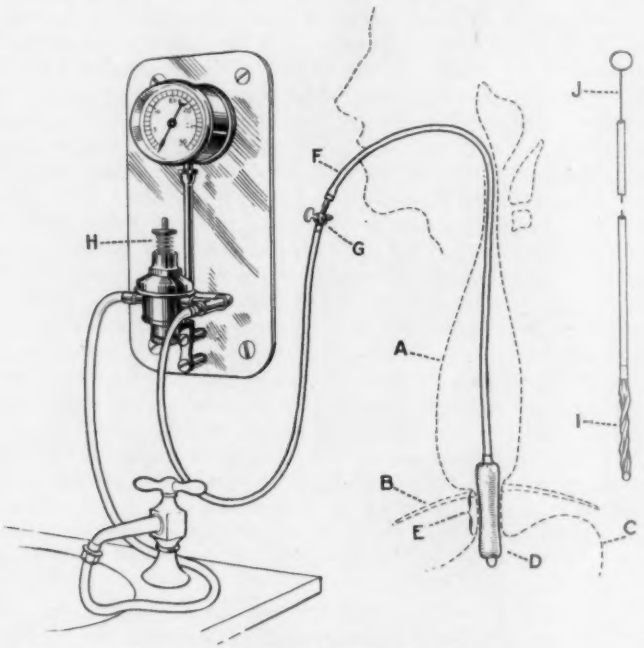

FIG. 5.—Author's apparatus for dilating the epicardia-cardia.

TREATMENT. The routine treatment of cardiospasm is the stretching of the lower end of the esophagus. This is done by introducing into the epicardia-cardia a silk-rubber bag (Russell) attached to a stomach tube and distending it forcibly with water or air, leaving the dilator *in situ* as long as the patient can stand it. As a rule, it cannot be endured more than a few minutes.

I make up the dilator in the following way: The distal end of a small-sized stomach tube with thick walls is closed and a number of holes are made in the lower four inches of the tube. Over this

is pulled an ordinary thin rubber condom, and outside of this a sausage-shaped bag 3 cm. in diameter and 15 cm. long, made of strong China silk. Both ends of the silk bag and the inner condom are securely fastened with a strong silk thread. Over the silk bag is pulled another condom to facilitate the introduction and prevent soiling of the silk bag.

The distance from the incisor teeth to the obstruction is noted and marked on the rubber tube. By the aid of a wire stylet (*J*, Fig. 5) the dilator is introduced into the epicardia-cardia and connected with the apparatus (Fig. 3), which is provided with a manometer and a pressure regulator (*H*). By slowly turning the screw of the regulator the pressure is gradually raised. The apparatus is modified from my first device, which I described in an article on Dilation of the Esophagus,[1] etc. About 10 pounds pressure is usually required for thorough stretching. When the dilatation is done the pressure is immediately relieved by turning the stopcock (*G*). The regulator prevents a sudden high pressure and the manometer is essential to keep track of the pressure. More than 15 pounds pressure is liable to burst the silk bag. Von Hacker found the average diameter of the adult cardia 35 mm., and that of the esophagus at the level of the diaphragm 24 mm., when the organ was filled with plaster of Paris or wax. Therefore, when the diameter of the silk bag is 30 mm. it is safe to use as high pressure as the silk bag will stand. It may perhaps be safe to dilate the epicardia-cardia to 35 mm., but I have had good results with the 30 mm. limit, and I feel safer in not exceeding this in view of the fact that the average diameter of the esophagus at the upper level of the diaphragm is 24 mm. I do not consider the patient's expression of pain a guide to the amount of pressure to be used. The fact that the dilator cannot expand beyond a known limit is the safety guide.

In several cases of cardiospasm of many years standing I have given the epicardia-cardia one or two stretchings, followed by other treatment required, with the most excellent result. It has been my experience that when cardiospasm recurs after repeated stretching other treatment besides stretching is indicated. The latter treatment is a painful procedure, and should not be repeated unnecessarily.

For the treatment[2] of the catarrhal condition of the mucous membrane of the esophagus I have been using nitrate of silver in solution, injecting it through a fine silver cannula, which has little holes on the sides near the distal end, but has the end closed. The cannula is inserted into a thick-walled rubber tube in order that it may be easily introduced without injuring the passage

[1] Amer. Jour. Med. Sci., October, 1907.

[2] Cuts of my instruments for application and other esophageal work appeared in Surgery, Gynecology, and Obstetrics, October, 1910.

(Fig. 6). The length of the instrument is 23 cm., so as to reach somewhat beyond the cervical portion of the esophagus. If ulcers are present they are best treated by direct applications through the esophagoscope of nitrate of silver melted on the applicator or of tincture of iodine.

For intra-esophageal application of the galvanic current in cases of atony of the esophagus I have devised an electrode, which can be introduced in a collapsed condition and expanded when it

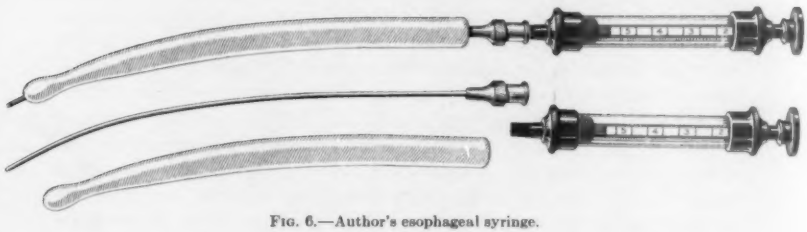

FIG. 6.—Author's esophageal syringe.

reaches the dilated part to be treated. The electrode collapsed and expanded is shown in Fig. 7, which illustrates well the working mechanism of the instrument, and the four thin steel springs (*A*) covered with felt to transmit the current. The handle is made of hard rubber and the long shaft of spiral steel wire is covered with a rubber tube.

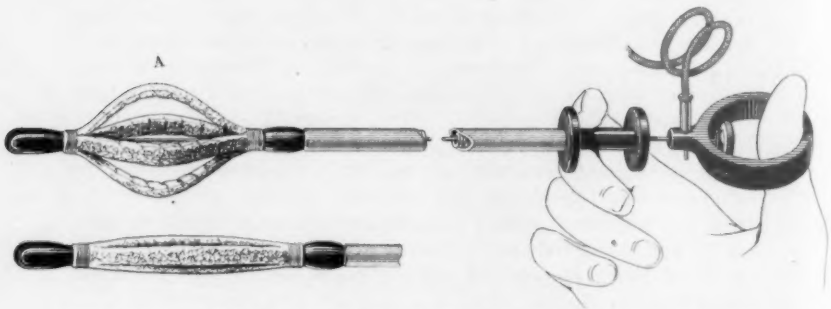

FIG. 7.—Author's esophageal electrode. Four thin steel felt-covered springs are shown at *A*.

The examination as well as the treatment by stretching in cases of cardiospasm can be done in the office.

Thoracotomy would, in my opinion, not be indicated unless the causative factor was definitely known to be in the thorax, and the simple treatment outlined above had failed.

Gastrotomy for mere stretching the epicardia-cardia is not justifiable, because more than one dilatation is often needed.

Furthermore, stretching performed through the mouth can be done quickly and without incapacitating the patient for work.

Seventeen cases of cardiospasm have come under my observation, and of these, 16 have been studied through the esophagoscope. For this article I have selected 4 cases, the first of which is the typical form of chronic cardiospasm. The other cases present features that differ somewhat from the ordinary.

CASE I.—Male, aged twenty-seven years. Ten years previous to consultation the patient had a choking spell while eating, with regurgitation of food. Ever since he has had difficulty in swallowing his food, and has had to take large quantities of water with which to force it into the stomach. He frequently gulped up food and slimy fluid. At times he had pain behind the lower part of the sternum.

Examination. Sounds met an obstacle at 42 cm. from the incisor teeth, which was passed without difficulty. The esophagus held more than a pint of fluid, and when the patient drank a couple of tumblerfuls of water he could regurgitate the whole amount a few minutes later, with the greatest of ease. The stomach contents was normal.

Treatment. The epicardia-cardia was stretched twice with the 3-cm. dilator. The patient has remained well since the last treatment, which was given four and one-half years ago. About three years after treatment I had the opportunity to examine the patient with the esophagoscope and found a perfectly normal appearing esophagus and the epicardia-cardia opened and closed rhythmically as in health.

The muscular tone of the esophagus must have been well retained in this case, because the patient could practically empty the organ by regurgitation after taking nearly a pint of fluid.

CASE II—Female, aged twenty-two years, unmarried. At the age of eighteen years, while eating a banana, a piece of it stuck in her throat. On drinking water it passed down. After this, whenever she ate, the patient noticed that the food would stick high in the chest and pass down slowly. Several months later it became difficult to get anything into the stomach and she had to take large draughts of water with which to force down the food. She had no pain, but an occasional burning sensation in the chest after gulping up mouthfuls of food and slime. She did not regurgitate often and it did not come easy, as it does in most cases of cardiospasm with dilatation.

Examination. Obstruction met 40 cm. from incisor teeth, which yielded to gentle pressure of the sound. Capacity of the dilated esophagus measured by the esophagometer was 400 c.c. *X*-rays (see Fig. 2) showed a sausage-shaped dilatation with the largest diameter in the upper thoracic part.

Esophagoscopic Examination. The mucous membrane was paler than normal, and near the epicardia it was deeper red than normal. The epicardia was closed. The upper thoracic part of the esophagus was ballooned out in an unusual manner, the like of which I have not seen in any other case.

Treatment. The epicardia-cardia was stretched several times with the 3-cm. dilator. The patient felt some relief, but was not entirely well; there was a sensation as if the food stuck in the upper part of the chest and passed down slowly. Repeated esophagoscopic examinations later on revealed the same ballooning of the upper thoracic portion of the esophagus as before.

The patient returned two years later in about the same condition. There was not so much obstruction to the passage of food at the lower end of the esophagus, but it passed slowly through the upper part. Esophagoscopic examination showed that the lower thoracic part had perhaps contracted somewhat, while the upper thoracic portion was in the same condition as it was two years previously. Although skeptical as to its value, I decided to try the application of the galvanic current intra-esophageally to the upper thoracic part, because this portion of the organ was undoubtedly in a state of atony. It would be impossible to bring an ordinary straight electrode in contact with the bulging walls of the esophagus, and I therefore, devised the above-described instrument (Fig. 7). After twenty applications esophagoscopic examination showed a surprising improvement, and after ten more applications the epicardia-cardia was stretched. Two months later esophagoscopic examination was made and the esophagus found practically normal, the cardia opening and closing rhythmically as in health. The patient felt entirely relieved. Seven months later esophagoscopic examination was again made and the organ found to be functionating normally. More than one year after treatment the patient was feeling perfectly well.

In this case there was primarily atony of the upper thoracic part of the esophagus, which delayed the passage of food and thereby irritated the epicardia-cardia to spasm.

Case III.—Female, aged twenty-three years, married, one child, three miscarriages, and one extra-uterine pregnancy, for which I operated upon the patient. One year after the extra-uterine pregnancy I performed supravaginal hysterectomy.

She had much trouble with her stomach in babyhood and was never strong. When aged ten years she was taken out of school on account of epigastric pain and belching of gas. At the age of sixteen years she experienced a severe cramp-like pain in the chest and between the shoulders. At the age of eighteen years, during the seventh month of pregnancy, she had a sensation of choking and oppression in the chest on eating, and shortly afterward she commenced to regurgitate her food. Occasionally she had pain

in the chest. At times fluid mixed with food came through the mouth and nose during sleep. She had been treated elsewhere by stretching of the cardia. The patient was fairly well for a while after the treatment, but the symptoms returned with regurgitation of food and severe attacks of pain. The pain would come on suddenly deep in the chest, radiating to the back between the shoulders and up the neck. Sometimes it was felt behind the

FIG. 8.—*X*-ray picture from Case III, showing relation of dilated esophagus to epicardia and stomach.

ears, particularly on the right side. The pain was cramp-like in character and so severe at times that repeated hypodermics of morphine would be required to relieve the patient. At times she felt as if everything in her chest was thumping. She had to take large quantities of water to get down her food.

Examination. Obstruction met at 40 cm. from incisor teeth, which offered some resistance to the sound. A considerable quantity

of slimy fluid with particles of food was drawn off. The capacity of the esophagus measured by the esophagometer was 500 c.c. The *x*-ray picture of the case (Fig. 8) is interesting because it illustrates beautifully the relation of the dilated esophagus to the epicardia and the stomach. It was due to an accident that this picture was obtained, the rubber bag containing the bismuth mixture dropped partly into the stomach.

Several esophagoscopic examinations were made and the mucous membrane showed signs of chronic and acute catarrh. On one occasion I found the upper two-thirds of the esophagus contracted, and the walls had to be pushed apart with the instrument. In the lower part above the epicardia was found about 100 c.c. of slimy fluid and the epicardia was firmly closed. The patient had just then had severe attacks of cramps in the chest, and the entire esophagus was apparently in spasm. At another examination I also noticed a tendency to contraction of the esophageal walls, but again on other examinations the esophagus was found open.

The epicardia-cardia was repeatedly stretched, which gave relief for a while. However, the spasms soon returned. Marital troubles and excitement would precipitate attacks, but, on the other hand, attacks came on without any apparent provocation. During the attacks I observed that the pulse was slow—about 60. I then tried the administration of $\frac{1}{150}$ grain of atropine sulphate three times daily for two weeks, with good result. There were no attacks of pain or regurgitation for several months. The use of atropine here was based upon the results of the experiments of Langley.[3] When the trouble recurred several months later it was in a mild form, with but little pain and only occasional regurgitation. Dilatation of the epicardia-cardia was again tried.

The patient subsequently died of pneumonia with complications. Partial postmortem was made and the esophagus found to be normal in size and appearance. On inflating the organ with air, however, it was found that it could readily be distended to several times its size, indicating that a dilatation had been present at a comparatively recent date.

My impression was that in this case there was an irritation of the pneumogastric nerve somewhere, but the neurotic temperament of the patient undoubtedly was an important factor.

Case IV.—Female, aged twenty-six years, unmarried. At the age of fourteen years the patient became subject to frequent attacks of a burning and gnawing sensation in the throat above the sternum and also behind the upper part of the sternum. The following year she noticed that coarser foods, such as corn, cabbage and beans, would stop in the chest, causing a sensation of pressure, and would then be regurgitated. In a few months liquids acted

[3] Jour. of Phys., 1898, Band xxiii.

in the same manner. She gradually learned to force the food down with water, and in the years that followed had no trouble with regurgitation so long as she took only a small amount of food at a time. She could not take iced water or charged drinks. The burning in the throat could be relieved on drinking cold water.

Examination. Obstruction met with at 42 cm. from incisor teeth, which did not permit the passage of the sound; 250 c.c. of slimy fluid with particles of food were drawn off. The capacity of the esophagus was 550 c.c. The *x*-ray picture (see Fig. 1) shows a pear-shaped dilatation with a pouch at the bottom.

Esophagoscopy. The esophagus appeared like a rigid tube with immovable walls. The greatest diameter was just above the epicardia, and the right wall of the organ was flattened out over the diaphragm, forming a pouch, the bottom of which the examining sound encountered. The mucosa was glassy white and edematous with red streaks here and there. The epicardia was so firmly closed that the esophagoscopic tube or the probe could not be pushed through. After the application of cocaine solution the epicardia opened. The mucous membrane of the latter was darker red than normal. The left wall of the esophagus was quite straight, so that the dilatation appeared to be more at the expense of the right wall.

Treatment. After one stretching with the 3-cm. dilator the patient reported four weeks later that there was no hindrance to the food whatever, but the burning in the throat continued unabated. I therefore commenced with daily injections of nitrate of silver solution into the upper thoracic part of the esophagus, but without any apparent effect. The injections were then made into the cervical part, and the patient soon reported decided improvement. She remained well for one year, with the exception of occasional burning sensations. She then noticed slight retention of food if she ate hurriedly. She therefore had another treatment by stretching, one and one-half years after the first treatment.

The cause of the severe burning in the throat, which acted like heartburn, is not clear, as the mucosa in the cervical part appeared quite normal. The chronic catarrh of the thoracic portion may have been the cause of it, but the decided improvement after the injections were made into the cervical portion made me think that the latter part was at fault. Shaffer has described "the upper cardiac glands of the esophagus," situated laterally in the upper end of the esophagus. These glands are of the same type as the acid-secreting cardiac glands of the stomach. The possibility occurred to me that these glands might have had something to do with the burning, but I could not demonstrate any reaction through the esophagoscope.

CONCLUSIONS. 1. If by cardiospasm is understood spasm of the anatomical cardia only, the name is not adequate.

2. The etiology of cardiospasm is obscure in some cases, and one should, therefore, be cautious in giving a prognosis.

3. Each case of cardiospasm must be studied *per se* and treated accordingly. Simply to demonstrate a spastic obstruction with the sound and stretch the epicardia-cardia is not sufficient in all cases.

4. The esophagoscope is paramount in making a correct diagnosis in any esophageal disorder.

The *x*-ray pictures have been taken for me by Dr. W. S. Fullerton, of St. Paul.

REVIEWS

SURGICAL APPLIED ANATOMY. By SIR FREDERICK TREVES, F.R.C.S., Sergeant-Surgeon to H. M. the King, late Lecturer on Anatomy at the London Hospital. New (sixth) edition, thoroughly revised. Pp. 676; 137 illustrations, of which many are in colors. Philadelphia and New York: Lea & Febiger, 1911.

TEN years ago we said of a previous edition of this work—revised then by the author with the assistance of Mr. Keith—that it was "prized by medical students for its lucidity, brevity, and, withal, its comprehensiveness." We added: "We know of no book between whose covers is compressed so much valuable information in such an attractive style."

The lapse of years has not made either of the above statements incorrect as applied to the present edition. Care has evidently been bestowed upon the revision and a number of additions have been made, but the clearness and precision of the original anatomical and surgical descriptions—to which it owed much of its success—are still noticeable. The defective proofreading of some of the earlier editions has been remedied and there is evidence of careful work in this direction. For example, the statement that the thyroidea ima artery "exists in 10 per cent. of all cases" is changed to "is found in one subject out of every ten."

As to additions, they are found chiefly, as the preface states, in relation to the glands of internal secretion, to the lymphatic system, to the anatomy of the abdomen, and to new facts regarding the human body that have been revealed by the *x*-rays. Taking illustrations almost at random, we find described the development and anatomy of the pituitary body and its relation to acromegaly and giantism; the pancreatic islets of Langerhans, and their bearing upon diabetic conditions; the suprarenal bodies, their growths and their involvement in renal tumors; the relations of stimulation of the laryngeal nerves to increased thyroid secretion; the atrophy and occasional disappearance of the parathyroids with advancing years; visceroptosis (with a diagram); the anatomy of the "Talma-Morrison operation;" gangrene of the intestine from embolism of the portal vein; and many other important and more or less recent additions to anatomico-surgical knowledge.

It is a pity that the diminishing but still noticeable tendency of many English surgeons to limit their field of inquiry to Great Britain and the Continent is not absent from this book. Many examples of this could be adduced, but we may mention the statement, under "Fractures of the Head or Neck of the Radius," that "the lesions if limited to the head could hardly be diagnosticated," no allusion being made to the enlightening research of T. T. Thomas; and the more important omission of any reference to the Allis method of reducing hip dislocations, the antiquated and dangerous plan of "circumduction" being the only one described. If in the next edition Mr. Keith will supply such deficiencies as these, the book is likely to remain for many years what it has been since its first appearance, the most admirable and useful condensation of the subject of applied anatomy in the English language. J. W. W.

DUODENAL ULCER. By B. G. A. MOYNIHAN, M.S. (Lond.), F.R.C.S. Pp. 179; 63 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

IN this monograph Moynihan has considered the subject of duodenal ulcer in an exhaustive and most interesting manner. The book consists of chapters upon ulceration in cases of burns or scalds, uremic ulcer, tuberculous ulceration, and the pathology, symptoms, diagnosis, and treatment of chronic duodenal ulcer, together with its various complications. This occupies 250 pages, and the remainder of the book, amounting to something over 100 pages, contains a detailed statement of all cases operated upon to the end of 1908.

There is but little to remark about in the book; it simply details in a complete and interesting way the phenomena of duodenal ulcer. The skill of the author as a surgeon is well known; he is one of the best of the abdominal surgeons of today, and his experience has been sufficiently great to make what he says authoritative. His skill is illustrated by his results; the mortality of the series of cases up to the end of 1909 was 1.6 per cent., and among the last 121 cases there were no deaths. Most of the cases were followed after operation, and it was found that practically 80 per cent. were cured, and only one patient was classed as being no better. One statement in the chapter on diagnosis (p. 112) should be memorized by every practitioner. He states that he has "never operated upon a case of retractive or recurrent 'hyperchlorhydria' without finding a duodenal ulcer." Another interesting statement is made when he says that he does "not believe in the duodenal ulcer which cannot be demonstrated to the most skeptical assistant or onlooker; the ulcer is always a visible, tangible, demonstrable lesion."

The only adverse criticism that might be made is that the size of the book could be materially reduced by eliminating the padding by unimportant case histories. Many of the illustrations are not up to the usual standard of the publishers. G. P. M.

A TEXT-BOOK OF MEDICAL DIAGNOSIS. By JAMES M. ANDERS, M.D., Professor of the Theory and Practice of Medicine and of Clinical Medicine, and L. NAPOLEON BOSTON, M.D., Adjunct Professor of Medicine, Medico-Chirurgical College, Philadelphia. Pp. 1195; 443 illustrations, 17 in colors. Philadelphia and London: W. B. Saunders Company, 1911.

To write a satisfactory work on medical diagnosis is a task of large proportions. Complete success has not, we believe, been accomplished in any first edition. The book before us is an attempt to present to the reader in reasonably condensed form the most approved modern methods of bedside and laboratory diagnosis, and this has, for the most part, been satisfactorily accomplished. The work is, nevertheless, susceptible of numerous improvements. Without wishing to be carping in our criticism we, however, feel that numerous additions, corrections, and alterations could advantageously be made in future editions.

We failed to find any allusion to sacro-iliac sprains, even in the discussion of lumbago, and no mention of cervical ribs. The modern classification of the cardiac arrhythmias receives but meagre consideration. No reference could be found to sinus arrhythmia, auricular fibrillation, pulsus alternans, nor to extrasystoles, although the latter is indefinitely alluded to in a brief paragraph on the "intermittent pulse." The statement that "the combination of symptoms known as 'heart-block' is only seen in cases in which the bundle of His is involved in a diseased process," requires modification, inasmuch as six or seven "exceptions" are on record.

We could find no mention of hepatic murmurs. Under sphygmographs only the obsolete Dudgeon and the Jacquet are alluded to. The time marker in the latter is said to record two-fifths instead of one-fifth of a second. The credit of devising the auscultatory method of determining blood pressure is given to "Karotskin," probably a misprint for Korotkow, while Fellner is not mentioned.

Under blood pressure only one type of instrument is alluded to. It would seem that the Erlanger and the Pachon instruments, at least, require mention. The determination of venous blood pressure should not have been ignored.

In discussing the newer methods of applying the tuberculin test the possible danger of the ophthalmic method should have

been mentioned, and the relative worthlessness of the v. Pirquet reaction in adults pointed out. For completeness the Moro reaction might have been included.

The index requires further elaboration. One seeks in vain for "pulsus paradoxicus," "vocal resonance," "pectoriloquy," and many other terms which must be sought under different headings. Kercher's name is spelled "Kearcher."

Pathological definitions heading the diseases are a useful addition to the text, but we question the advisability of introducing so many space-consuming "illustrative cases." The anatomical reasons for the normally greater right-sided pulmonary tactile fremitus should have been mentioned.

The chapters on diseases of the nervous system and Röntgenology are written by T. H. Weisenberg and G. E. Pfahler respectively, and are, so far as the reviewer's limited knowledge goes, satisfactory.

The work is attractively gotten up, with good print, many excellent illustrations, and with tables of differential diagnoses, which are probably useful for students. Among the illustrations the introduction of moving pictures in different nervous diseases may be mentioned. On the whole the aim of the authors to combine a description of different methods of physical, clinical, and laboratory diagnosis as available for different pathological conditions has been successfully consummated. G. W. N.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital, etc., Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. IV; pp. 326; 35 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

THE final volume of *Progressive Medicine* for 1911 opens with a painstaking review of diseases of the digestive tract by R. S. Lavenson. After he considers the esophagus, he takes up the pathological physiology as well as the diseases of the stomach. He then discusses diseases of the intestines. That appendicitis continues to excite interest and controversy is evident from the amount of space devoted to this subject. The peritoneum, the liver, and the biliary tract are next considered, particular emphasis being laid upon cholelithiasis. Lavenson's article of 92 pages concludes with a discussion of diseases of the pancreas.

A short contribution of 15 pages on diseases of the kidneys is furnished by John R. Bradford. The function of the glomerulus, the genesis of dropsy in heart disease and in Bright's disease, and a summary of the efficacy of urinary antiseptics, are among the important subjects covered in this contribution.

Genito-urinary diseases proper are thoroughly discussed by Charles W. Bonney in an article 45 pages in length. Functional renal diagnosis, unilateral hematogeneous infection of the kidneys, gonococcic infection of the kidney, and tuberculosis of the genito-urinary tract; intraperitoneal rupture, tumors and tuberculosis of the bladder; together with an extensive discussion of hypertrophy and carcinoma of the prostate and various conditions of the external genitalia are among the most important subjects considered.

A truly critical review of certain phases of general surgery is contributed by Joseph C. Bloodgood. Under the title of injuries this writer enters into an excellent discussion of shock and anesthesia, paying particular attention to the anatomical basis of shock as advocated by Crile and his associates, and to nitrous-oxide-and-oxygen anesthesia, which, it would appear, continues to gain in favor. A consideration of wounds, infections, lymphangitis, lymphadenitis, tetanus, and tumors is followed by a discussion of fractures, bone tumors, and advances in the surgery of the lymph glands.

The volume ends with an interesting contribution of 43 pages by H. R. M. Landis upon recent progress in therapeutics. In this distinctly practical chapter, Landis takes up not only the newer ideas in regard to drugs, but also lays particular emphasis upon such valuable therapeutic measures as rest, climate, diet, exercise, massage, hydrotherapy, and serum and vaccine therapy.

Considered as a whole, the four volumes of *Progressive Medicine* that have appeared during the past year furnish, without a doubt, the most complete and useful critical review of present-day medical thought that can be found in English. G. M. P.

THE PRINCIPLES AND PRACTICE OF BANDAGING. By G. G. DAVIS, M.D., Member of the Royal College of Surgeons, England; Professor of Orthopedic Surgery, University of Pennsylvania. Third edition; pp. 128; 164 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

THE author has given in this book an excellent explanation and illustration of bandaging. This the third edition is practically a new book, being rewritten from the older work. It is especially

designed for beginners and is, for that reason, well recommended for the use of students.

The text is clear and the style agreeable for a book of this sort. The illustrations clearly show what is fully explained in the context, and, being original with the author, point out admirably the points difficult for beginners. Every important bandage has a cut showing the turns and the method of application step by step. Brief mention is made of rubber and plaster of Paris. The handkerchief or triangle bandage is discussed and illustrated at great length.

For students, this work is most complete and easily on a par with any other work on the same subject. It is of a handy size and the type is clear and easily read. The placing of numbers on the various turns of the bandage in the difficult figures renders it much easier to master the method of applying the bandage illustrated.

E. L. E.

THE MODERN DIAGNOSIS AND TREATMENT OF DISEASES OF CHILDREN. By HERMAN B. SHEFFIELD, Instructor in Diseases of Children at the New York Post-Graduate Medical School and Hospital, etc. Pp. 619; 150 illustrations. Philadelphia: F. A. Davis Co., 1911.

THIS book, like the previous contribution of the author (the translation of Graetzer's *Pediatrics*), contains a generous amount of useful information. Unlike the earlier work, however, the present volume has its subject matter well arranged; it is well written; it is illustrated; most of the illustrations are original and most of them are excellent. In the main, the tone of the work is thoroughly scientific, and the newer methods of diagnosis and treatment are clearly and concisely described. The use of prophylactic and curative sera and of vaccines is dealt with in a judicial manner. The book making is well executed and the type is large and clear.

We detect few important omissions and fewer mistakes. Although he speaks of the importance of light percussion in children, Sheffield does not mention the value of finger-nail percussion in the young, nor does he lay stress upon the still more important matter of the "resistance" offered to the pleximeter. He does not differentiate between Cheyne-Stokes respiration and grouped cerebral breathing.

Although he does use the adjective mammary, as applied to the nipple line, instead of the questionable adjective mammillary, we find him describing the iliac region as the inguinal region. Others have objected, as do we, to so extending the limits of the groin.

The author deals with the subject of rectal examination, but he does not lay enough stress upon the digital examination of this

important region, nor does he mention all of the clinical findings that may be so elicited.

In the directions for making buttermilk, nothing is said about churning the soured milk. Thus the butter fats are left in, at least one is allowed to suppose so, and the resulting product is not buttermilk.

The Wassermann reaction, of which a full and lucid account is given, is not found in the chapter on "Diagnosis," but in that dealing with the "Treatment and Cure of Disease." The same criticism may be made of the description of the Widal reaction. Some minor objections might be advanced to the arrangement of the "Communicable Diseases." Thus we find diphtheria "sandwiched" between two of the exanthemata—scarlet fever and measles.

We should hesitate to believe that masturbation is often taught children by "erotic governesses," though we would admit that it is sometimes taught them by ignorant or vicious nursery maids.

However, most of the criticisms are minor ones, and we find little to invalidate the usefulness of the book. It is a good book, and we recommend it cheerfully to students and practitioners.

J. H. McK.

A Manual of Materia Medica for Medical Students. By E. Quin Thornton, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College, Philadelphia. Pp. 525. Philadelphia and New York: Lea & Febiger, 1911.

Thornton's *Materia Medica* is a highly useful book, both for the practitioner and the student of medicine. It is divided into three parts: The first deals chiefly with the principles of prescription writing; the second contains the official remedies arranged alphabetically according to source and derivation; the third is a strictly alphabetical table of all the official preparations. In the second part the methods of preparation, the physiological and toxicological actions, and the uses of the various remedies are described in a strictly objective way, without any comment as to their relative value. This part will be found exceedingly useful by the practitioner who wishes to inform himself quickly as to the action and dose of a drug, and of the best way to administer it. The last feature, about which the medical profession is generally quite ignorant, receives careful attention in the case of nearly every preparation. An occasional non-official remedy is introduced, as for example salvarsan. Considering, however, the extensive employment of synthetic compounds, many of which possess unquestioned value, it would enhance the usefulness of the book if in future editions a section on these newer unofficial remedies was added.

D. R.

CASE HISTORIES IN NEUROLOGY. By E. W. TAYLOR, A.M., M.D., Instructor in Neurology, Harvard Medical School; Assistant Physician, Department of Neurology, Massachusetts General Hospital; Visiting Neurologist, Long Island Hospital, Boston. Pp. 305; 37 illustrations. Boston: W. M. Leonard, 1911.

IN brief, this book contains histories of more or less typical cases of nervous disease which are presented first as to history, then diagnosis, and finally, prognosis and treatment, and which are used by the medical students of Harvard University. The reviewer has known of this work for a number of years and from personal knowledge knows that the case history system has been instrumental in good work. This method has also been used in other specialties such as pediatrics and in medicine and surgery and is to be heartily commended. T. H. W.

CLINICAL PATHOLOGY IN PRACTICE. By THOMAS J. HORDER, B.Sc., M.D., F.R.C.P. Pp. 216. London: Oxford Medical Publications, 1910.

THE task of the reviewer lies, not infrequently, in unpleasant pastures, beside waters that he feels should be dammed, which, were his preferences consulted, he would have done by someone else. The present reviewer keeps continually before his mind the fact that any book, no matter how small, is conceived of no hasty thought, and is born after much wearisome and fatiguing travail. He remembers this, and tries to view even a misshapen child, as the parent views it, with a kindly eye, seeing naught of its ugliness, but affectionately emphasizing each good trait.

The work at present under consideration has for its object "to present the practitioner with a brief survey of the scope and usefulness of modern pathological methods as applied to the diagnosis and treatment of disease." An introduction of nine pages is then devoted to a defence of laboratory methods and to an attempt to point out the proper correlation of the findings of the clinician and of the laboratory worker. Both the aim of the book and the introduction seem to us as smacking of a very early era in medicine, and as not being apropos in this day of our generation.

Granting that the aim of the author is a praiseworthy one, we fail to see that he hits the mark. Occasionally he strikes the target, but they are glancing shots, and do no one much good. We might cite instances of these stray half-hitting attempts, but they must be apparent to every one.

The volume presupposes ignorance on the part of the clinician

as to the features which should be studied in a case, and it shyly hints at what might prove of help. These hints leave us with the sensation of being suspended in midair, as it were, since we can not find a footing for our scientific groping feet. A much better idea of the usefulness of the application and advantages of clinical pathology is to be had from any of the numerous works devoted to this department of medicine. E. H. G.

MENTAL MECHANISMS. By WILLIAM A. WHITE, M.D., Supt. Government Hospital for the Insane, Washington, D. C.; Professor of Nervous and Mental Diseases, Georgetown University, Washington, D. C.; Professor of Nervous and Mental Diseases, George Washington University, Washington, D. C.; and Lecturer on Insanity, U. S. Army and U. S. Navy Medical Schools. Pp. 515. New York: Journal of Nervous and Mental Disease Publishing Co., 1911.

As the author states in his preface, "This work is the result of a need growing out of my efforts to bring certain principles in the field of psychology to the younger members of my staff," and is an excellent presentation of the modern trend of psycho-analysis. The author has the gift of clear concise expression, and one who is not familiar with psycho-analysis, especially Freud's methods, will gain much from perusal of this work. T. H. W.

LEITFADEN DER ELECTRODIAGNOSTIK UND ELECTROTHERAPIE, VON DR. TOBY COHN, Nervenarzt in Berlin. Pp. 212; 65 illustrations, 6 colored plates. Berlin: S. Karger, 1912.

THE popularity of this little guide is obvious from its previous translation into English, Italian, and Russian. In this fourth edition, the text is entirely rewritten and considerable new matter is added. Mention is made in the preface, of the author's writings in collaborate works, upon electricity in conjunction with mechanotherapy (massage and gymnastics), but the latter is not considered in this text.

The section on electrodiagnosis contains six admirably arranged colored plates, with transparencies showing the motor points upon the surface of the body. We know of but one series of plates that are superior, and these are found in Mosher's *Electrodiagnosis*, where nerve and muscle groups are classified by means of colored

stars which represent the nerve points, and correspondingly colored circles which signify the muscles supplied.

The section on electrotherapeutics contains most of the new matter. Of the two types of static machine, the Wimshurst is preferred, this is not the machine of choice in this country. The uses of the static current are considered under the headings of breeze, head-douche, air-bath and sparks (*a*) as a means of massage, etc., (*b*) Morton's static induction current and wave current. The high frequency current has grown but little in favor since the preceding edition.

The final chapter considers the newer forms of current and of these the only one that has so far come into general practice is the sinusoidal current; this, with its modifications, the author regards as physiologically like the faradic current, though milder and a little less painful.

The slowly spreading use of Leduc's rhythmically interrupted galvanic current, and the condensation discharge, Cohn deplores, and says "both currents shall certainly be called upon in the future to play an important role in electric medicine." The only American physician whom we see mentioned is W. J. Morton.

This little work is written by an acknowledged authority, and its usefulness is shown by its having appeared in four languages, together with the call for this fourth edition. N. S. Y.

Compendium of Regional Diagnosis in Affections of the Brain and Spinal Cord. A Concise Introduction to the Principles of Clinical Localization in Diseases and Injuries of the Central Nervous System. By Robert Bing, Privat-Dozent for Neurology in the University of Basle. Translated by F. S. Arnold, B.A., M.B., B.Ch. (Oxon). Revised by David I. Wolfstein. Pp. 215; 70 illustrations. New York: Rebman Company, 1911.

It is indeed a pleasure to review this book, for the original in German is very well known to neurologists. The translation and revision has been well done and is fully up to the original.

This work is unquestionably the best small work on neurology printed in any language. It contains the essence or groundwork of neurology, and has the exceptional merit of being well and clearly put forth, so that the reader has no doubt as to the author's meaning. Besides, the illustrations are splendid and have that rare qualification, that is, they explain. It is distinctly the best work on organic neurology for students and general practitioners.

T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Functional Diagnosis of the Liver.—F. Falk and P. Saxl (*Zeitsch. f. klin. Med.*, 1911, lxxiii, 325) publish their second communication on functional liver diagnosis. For purposes of study they have divided affections of the liver into four groups. Group I includes tumors of the liver like cancer, sarcoma, ecchinococcus, amyloid liver, leukemia, and chronic passive congestion. The parenchyma is affected secondarily. In Group II they place all infections and intoxications (typhoid, pneumonia, tuberculosis, chloroform, alcohol, phosphorus, for example). The third group contains those conditions in which the liver may be pathologically affected by the escape of bile from its normal passages (icterus from gallstones, from complete closure of the common duct, and from catarrhal conditions). In Group IV are placed the atrophic and hypertrophic cirrhoses of the liver. As functional tests, Falk and Saxl employed only those of known value, *i. e.*, levulose, urobilin, and the nitrogenous bodies—amino-acids, polypeptids, ammonia. Each of these tests was applied to their cases. The analysis of their results and of those reported in literature shows that a marked disturbance of liver function is disclosed, particularly in cirrhosis of the liver. Nitrogen ratios, urobilin excretion, and tolerance for levulose all reveal abnormalities. Such constancy of findings is seen in no other hepatic disease. In Falk and Saxl's cases these disturbances of function appeared early in the course of the disease. Often it was possible, by finding urobilinuria, levulosuria, and especially abnormal nitrogenous ratios, to arrive at the correct diagnosis at a stage of the affection when only vague gastric symptoms were present. In the remaining three groups the findings were less useful in a diagnostic way.

On Apical Rales.—Külbs (*Zeitsch. f. klin. Med.*, 1911, lxxiii, 169) has observed a number of patients with symptoms and signs suggesting pulmonary tuberculosis, which proved to be non-tuberculous. The symptoms complained of were shortness of breath on exertion, anorexia, and lassitude. Objectively, it was observed that the nutrition of the patients was only fair, excepting a few adipose individuals. The temperature remained normal. The examination of the internal organs revealed nothing unusual with the exception of the lungs. Here there was almost constantly a roughened (at times a diminished) vesicular breathing with prolonged expiration, usually heard over the right apex posteriorly, seldom over the left apex posteriorly or over the right anteriorly. In addition to these changes, medium-sized moist or dry rales were audible quite constantly in the same regions. The expansion was diminished, but without unilateral decrease. Röntgenographic study gave normal apices, not a sign of infiltration being found. In the cases subjected to tuberculin a positive reaction was not obtained. In one-half of the cases a mucoid sputum was expectorated; in all of these (11 cases) repeated examinations failed to reveal the tubercle bacillus. The patients were all young (under thirty-five years of age). Examination of the throat often showed a chronic pharyngitis, laryngitis, and tracheitis. With the subsidence of the latter, the pulmonary signs, which the author interprets as evidences of a chronic, non-tuberculous bronchitis, usually subsided or entirely disappeared.

The Destruction of Hemoglobin in the Liver.—L. Hess and P. Saxl (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 1) have previously shown that the livers of white rats and rabbits, when subjected to aseptic autolysis, destroy their own hemoglobin so completely within a few days that the absorption spectrum of oxyhemoglobin entirely disappears. On the other hand, livers from animals that had been poisoned with yellow phosphorus, arsenic, strychnine, caffeine, chloroform, morphine, diphtheria toxin, adrenalin, pilocarpin, and strophanthin exhibited a marked retardation and diminution in their power to destroy hemoglobin. Such livers remained deep red for weeks, and quantitative determinations of hemoglobin showed a very slow reduction in quantity. Of the poisons enumerated, arsenic, phosphorus, chloroform, diphtheria toxin, and adrenalin are known to produce anatomical lesions in the liver, while strychnine and morphine are rendered nontoxic in the same organ. Caffeine may cause a glycosuria, but is otherwise without known effect on the liver. Since all the substances had the same effect on autolysis of the liver, Hess and Saxl believed they were dealing with an elective disturbance of the function of destroying hemoglobin. This supposition was the more likely, since the postmortem addition of these compounds was without any effect upon hemoglobin destruction. These studies led to similar observations on the human liver, in an effort to learn more of the pathology of hemoglobin destruction. Livers were obtained as soon as possible after death, and subjected to aseptic autolysis. Hess and Saxl found that the hemoglobin was completely destroyed within ten to twenty-five days in pulmonary tuberculosis (3 cases), scarlet fever (1 case), pneumonia (2), incarcerated hernia (1), cholera infantum (2), sepsis (2), measles,

leukemia, typhoid fever, diphtheria, phlegmon, meningitis, capillary bronchitis, erysipelas, and brown atrophy of the liver with cancer (each 1 case). On the contrary, there was slight destruction or none in pneumonia (5 cases), vitium cordis (2), gastro-enteritis (2), cancer of the liver (2), pulmonary tuberculosis (1), hereditary lues (2), measles, liver abscess, scolicoiditis, otitis media, cancer of esophagus, endocarditis, tuberculous meningitis, arteriosclerosis, scarlatina, diphtheria, lysol poisoning, and cirrhosis (1 case each). The inconstancy of the results Hess and Saxl attribute to the supposition that, as in the case of drugs, functional disturbance may be produced without anatomical lesions, and that a given disease does not affect the liver to the same degree in each instance. Reviewing the literature and analyzing their own material, Hess and Saxl show that with anatomical or functional disturbances of the liver, a polycythemia is at times observed, a result which one would anticipate if the hemoglobin destruction were diminished below the normal. Finally, to bring forth more evidence, Hess and Saxl served as experimental persons, and, after establishing their normal blood counts, observed the effect of various drugs on the number of their erythrocytes. The observations extended throughout a year. A marked increase, up to 7,000,000 was found after tincture of opium. Definite but less striking figures are reported following Fowler's solution, caffeine, strophanthus, and cognac. The increase in cells was gradual, reaching its maximum in ten to fourteen days. These results are interpreted as evidence of the inhibitory action of the above-named drugs upon the hemoglobin-destroying function of the liver.

The Adrenalin Content of the Adrenal Glands.—A. INGIER and G. SCHMORL (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 125) have made quantitative determinations of the adrenalin in the adrenal glands in a series of 517 cases. Their exhaustive study adds much valuable information to a field which is none too well illuminated. Their observations cover such a wide range of material that it is possible to indicate the results only by quoting their summary: (1) In the examination of 517 patients at autopsy, the average adrenalin content of both adrenals was 4.22 mg. Up to the age of nine years the adrenalin averaged 1.52 mg.; between ten and eighty-nine years the average was 4.59 mg. (2) During the first few years of life the adrenalin content gradually increases, but from the tenth year onward there is little variation. (3) In the diseases studied, the adrenalin varied within relatively narrow limits. (4) In the infectious diseases, a decrease of adrenalin was not demonstrable as a rule. (5) In atherosclerosis, the amount of adrenalin was only slightly augmented. (6) In acute nephritis, contracted kidney (including chronic nephritis), and in chronic cardiac diseases, an increase beyond the average adrenalin content was demonstrable. (7) In Addison's disease the adrenalin in the adrenal glands was nil. (8) Diabetes gave a somewhat diminished quantity of adrenalin. (9) In status thymolymphaticus a slight decrease was seen in the majority of the cases; sudden death in this condition cannot, however, be attributed to an exhaustion of the chromaffin system. (10) In cases of sudden death (as from violence) an increased quantity of adrenalin was observed in most instances, but not with sufficient constancy to give diagnostic value to the finding. (11) When death followed within twenty-four hours after

narcosis, the amount of adrenalin was somewhat subnormal. (12) When death followed convulsive seizures, the quantity of adrenalin was also below the normal. For the quantitative determinations of adrenalin, Ingier and Schmorl modified Comesatti's method, using adrenalin (Takamine) solutions as standards. Histological examinations of the chromaffin tissue were also made.

The Bacteriology of the Cockroach.—C. Conyers Morrell (*Brit. Med. Jour.*, London, 1911, ii, 1531) describes the life history of cockroaches, their method of feeding and growth, and then mentions experiments conducted bacteriologically. Animals were kept aseptically until defecation occurred, then cultures were made from the feces, with resulting growth of Bacillus lactis aërogenes, Bacillus cloacæ, and moulds of the Aspergillus variety. In order to prove the transmission of known organisms, animals were fed tubercular sputum, pus containing staphylococci, and aspergillus spores. Tubercle bacilli (identified by staining reaction) were present in the feces passed within twenty-four hours of feeding. Cultures of both organisms and mould were obtained from the feces of the pus and spore-fed animals. Morrell concludes that the common cockroach is able, by contamination with feces, to bring about the souring of milk, to infect food and milk with pathogenic organisms, and thus possibly to become a dangerous domestic pest.

A Cutaneous Reaction in Syphilis.—Hideyo Noguchi (*Jour. Exper. Med.*, 1911, xiv, 557) has prepared from pure cultures of Treponema pallidum, a substance analogous to tuberculin, to which he has given the name "luetin." The spirochetes are grown at 37° C. for periods of six, twelve, twenty-four, and fifty days, anaërobically, on a medium of ascitic fluid, or ascitic fluid agar containing placenta. The agar cultures thus obtained were ground, and the resulting thick paste was gradually diluted, until the emulsion became liquid. This preparation was heated to 60° C. for an hour, and 5 per cent. carbolic acid added. When examined microscopically, 40 to 100 dead pallida were found per field, cultures from which showed no growth. A similar emulsion with uninoculated medium was used for control. "Luetin" was tested experimentally, with the observations that repeated inoculations of either living or killed pallida into testicles of rabbits lead to a condition in which an intradermic injection of luetin in dosage of 0.05 c.c. was followed by a well-marked cutaneous reaction. A corresponding reaction was not obtained in normal animals, in those suffering from active syphilitic orchitis, or in those in which the condition had been cured by the administration of salvarsan four months previously. Luetin was tested similarly on 177 syphilitic cases; 77 parasyphilitic, and 146 control patients. No marked constitutional effect was noted beyond slight fever or malaise. Control cases showed no reaction. In positive cases the reaction was: (1) Papular, appearing in twenty-four to forty-eight hours, developing induration lasting about a week. (2) Pustular, at first resembling the former, but after four or five days progressing to pus formation. (3) Torpid form, resembling negative cases, but suddenly after ten days or more lighting up. The analysis of the human cases showed that in cases of primary or secondary syphilis, which had had either insufficient treatment or none at all, no

skin reaction occurred except in a few instances. In the positive cases the reaction was always papular. On the other hand, most secondary cases which had been mercurialized before the administration of salvarsan, or which had remained without symptoms for some months after salvarsan injections, gave striking and unmistakable reactions. The reactions in tertiary or hereditary syphilis were the most intense, and appeared more constantly than the Wassermann reaction. On the other hand, syphilis of the central nervous system reacted positively to luetin, less constantly than to the Wassermann. Among cases treated with salvarsan, two groups gave negative or doubtful reactions, the one doubtful, in those cases without symptoms, but with the reappearance of the Wassermann reaction; the other always negative, in cases that remained without clinical symptoms or Wassermann reaction for many months. In conclusion Noguchi states that it remains to be determined in how far the cutaneous reaction can be used to supplement the Wassermann test in determining the complete and permanent suppression of syphilitic infection; it appears probable, however, that the Wassermann is more constant in primary and secondary disease; the cutaneous in tertiary and latent syphilis.

The Experimental Production of Appendicitis by the Intravenous Injection of the Diplococcus.—F. J. POYNTON and ALEXANDER PAINE (*Proc. Roy. Soc. Med.*, London, 1911, v, Path. Sect., p. 18,) describe experiments with a culture of a diplococcus obtained from the knee-joint of a boy with acute articular rheumatism, who later, under salicylate of soda, made complete recovery. Twenty-four young rabbits were inoculated intravenously in varying doses, either with the original or subcultures. Of these, 4 developed, in addition to arthritis and mucous diarrhea, an acute appendicitis of varying severity, involving the outer half of the appendix. Histologically, transitions were found from the earliest stage of infection by the blood stream, with the first changes appearing in the mucous and submucous coats, to complete destruction of normal tissue, ending either in necrosis, minute ulcer formation, or the early connective tissue proliferation of healing. Diplococci were visible within phagocytes. In one case early manifestations of general peritonitis were present with living organisms in the peritoneal fluid, yet without signs of perforation. In another, there was a ballooning of the affected area, suggesting the possibility that in man some such loss of tone may favor the stagnation of secretions and contents, with resulting concretion formation. In no cases were there other visceral lesions. Ten years ago, Adrian reported similar cases of experimental appendicitis in rabbits, produced by the intravenous injection of streptococci, staphylococci, pneumococci, typhoid, and colon bacilli. He does not mention the source of the organisms used nor describe any ulcer formation, or accompanying lesion such as arthritis. He reviews the literature of the subject. Poynton and Pain conclude that the histology of these and many human cases are very similar. The association of arthritis, mucous diarrhea and appendicitis is interesting, in its bearing on auto-intoxication from the bowel as a cause of arthritis. These observations make it seem possible that all lesions may be the result of a primary cause circulating in the blood stream and determining to these various positions.

SURGERY

UNDER THE CHARGE OF

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The Choice of the Method of Exposing the Heart for Suture.—KÖNIG (*Deutsch. Zeitsch. f. Chir.*, 1911, cxii, 490) says that it is desirable, in exposing the heart for suture, not only to employ a typical method, but to have regard for the special circumstances of the particular case. When there is a penetrating wound to the right of the sternum, a sternal method should be used without exception. All methods which remove a part of the sternum only are time consuming and not easily performed, so that they are dangerous and to be avoided as much as possible. Extrapleural methods, where the pleura is intact, are to be unconditionally preferred, but where the pleura is already wounded, the transpleural method is to be preferred, if no time is to be lost by it. The approach to the heart must be as wide as possible, the disturbance in the firmness of the thorax as slight as possible. The method which provides these requirements best is the Kocher, especially for wounds between the left sternal border and the mammary line. The horizontal portion of the incision passes from the left chondral junction along the cartilage (second to fourth, according to the necessity), the vertical portion along the middle of the sternum, and the oblique portion along the sixth costal cartilage, the included cartilages being resected. When the heart wound is external to the mammary line, the Rotter flap is to be preferred, because by it a direct canal can be followed to the wound in the heart. This flap has its base at the left border of the sternum, is rectangular, extends outward to beyond the mammary line, and from the third to the fifth rib.

Recurrence of Ulcer of the Stomach after Gastro-enterostomy.—FINK (*Zentralbl. f. Chir.*, 1911, xxxviii, 1497), on November 16, 1908, did a posterior gastro-enterostomy on a man, aged forty-three years, in whom he found an ulcer involving the anterior and posterior walls and lesser curvature; and these were adherent to the liver. The ulcer had a characteristic appearance and was associated with a considerable dilatation of the stomach. After the gastro-enterostomy the symptoms disappeared, the patient gained strength and put on weight. He returned to work, looked well, and could take all kinds of food without care or choice. This condition lasted two years. For four weeks

he had been suffering from marked symptoms of ulcer, with severe bloody vomiting on two occasions, and marked loss of weight, when, on December 29, 1910, Fink again opened the abdomen. There was found at the same place as in the first operation a callous ulcer, which had incompletely occluded the pylorus and was associated with a slight dilatation of the stomach. At the site of the gastro-enterostomy, the jejunum was adherent to the stomach for not quite 10 cm. The communicating opening between the two could not be felt. The ulcer-bearing area in the pyloric region was removed for about 10 cm. and the stomach closed by direct apposition. On examination through the resection opening, the communicating aperture with the jejunum could not be seen. The healing after the second operation was uneventful, and the patient did well. Fink saw a causal relationship between the closure of the gastro-enterostomy opening and the recurrence of the ulcer. In the first place the passage of the stomach contents through the new opening relieved the ulcer of irritation, so that it slowly healed. The stenosing effect of the ulcer upon the pyloric opening being removed, this aperture gradually assumed its normal proportions, so that the food could again take its physiological course through the pylorus. The gastro-enterostomy opening then having no work to do, closed. The conditions favoring the reëstablishment of the ulcer were again present. Its development with inflammation of the surrounding tissues brought about a relative pyloric stenosis and consecutive extension of the ulcer and hemorrhage. According to the evidence in this case, closure of the gastro-enterostomy opening is to be expected in every case of ulcer which, as it does not lie directly at or near the pylorus, gives rise to only a relative stenosis; so that after the ulcer has healed the stomach contents can be emptied in the normal manner. In these cases of ulcer recurrence after gastro-enterostomy Fink recommends the operation of excision of the ulcer.

The Importance of the Inhalation of Oxygen in Thoracic Surgery.—TIEGEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 1529) says that in a previous communication he called attention to a simple and practical principle in thoracic surgery. The chief danger of an operative pneumothorax lies in the insufficient ventilation of the lung, and the resulting deficiency in oxygen. Tiegel says this can be best overcome by the inhalation of oxygen. A man may preserve a sufficient respiration, even with an open pneumothorax, so that he will do much better if oxygen is substituted for air. This will raise the depressed respiratory exchange fivefold. Animal experimentation demonstrates this by showing that the inhalation of oxygen under a minimal pressure (1 cm.), which does not distend the lung, gives a better arterialization of the blood than occurs with the usual differential pressure. Tiegel has employed this method in a number of cases, and has observed no disadvantages from it, even in long continued operations. There was no dyspnea or cyanosis during the operations on the collapsed lungs. This among many others was the most important technical advantage. The great superiority of the use of oxygen over the air pressure is shown by the following experiment: A young dog was given intravenously 5 mg. of a tuberculous culture (human type). Some months later the dog was very much emaciated, and exhibited marked dyspnea. Narcosis

was conducted under oxygen inhalation, whereupon the dyspnea was improved. An incision was made, and the blood found to be bright red. For economical reasons, a differential pressure with air of about 12 cm. (overpressure), was maintained. The lung, which showed high-grade tuberculous changes, remained filled and in close contact with the chest wall. Yet the breathing was dyspneic and the blood cyanotic. It was suspected that this was due to a closing of the glottis by a falling backward of the tongue or epiglottis, but this was disproved by the rhythmical movement of the gas bag. Because the dyspnea increased to the point of threatening suffocation, Tiegel, keeping up the same pressure, substituted oxygen for the air. Immediately the dyspnea improved and the blood became bright red. The dog died soon after the operation, and an examination showed an extensive tuberculosis of both lungs.

The Treatment of the Duodenal Stump in a Gastro-enterostomy by the Billroth II Method.—Fáykiss (*Zentralbl. f. Chir.*, 1911, xxxviii, 1532) advises the following method of overcoming the difficulties associated with the closure of the duodenal stump: After careful closure of the stump by means of a suture including all the coats, he sutures the pancreas over it. When possible he includes in the suture the peritoneal covered portion of the duodenum, and if the stump is too short to permit this the posterior parietal peritoneum is employed. The fine intestinal needle must grasp the pancreas, superficially, and the great bloodvessels must be avoided. Finally, the covering of the stump by the pancreas must be complete. The operation works well also in those cases in which, with the tumor, a part of the pancreas must be removed. This happened in two cases in which the wounded surface of the pancreas was made to cover the duodenal stump. Fáykiss employed this method in 6 cases. It was successful in all, the healing being good and no fistula occurring.

Anesthesia by Intratracheal Insufflation.—Cotton and Boothby (*Surg., Gyn., and Obstet.*, 1911, xiii, 572) say that the technical difficulties of intubing the trachea have prevented, in all but the most enthusiastic hands, the application of Meltzer and Auer's intratracheal insufflation anesthesia. Cotton and Boothby have devised an introducer, in curve and angle, following nearly the O'Dwyer intubing apparatus, in use being rather different. When the patient is etherized fully with inhaler or cone, a mouth gag is inserted on the patient's left, the tongue is dragged forward sharply with tongue forceps, the operator's left index finger is thrust down until it meets the epiglottis, and the "introducer," held in the right hand, is pushed in and down, alongside the left forefinger, till it has passed the upper projecting edge of the epiglottis. Then the heel of the instrument is pitched upward, and the assistant feeds the catheter into the larynx and trachea. The curved end of the "introducer" is tubed for the passage of the catheter through it, in order to prevent buckling of the rubber tube. At first nitrous oxide was given with the usual oxygen co-efficient till consciousness was lost, and anesthesia was then deepened by the addition of ether till the laryngeal reflex was abolished and when the intratracheal tube was introduced. No air was used, only nitrous-oxide-oxygen-ether.

Presently the ether was cut off, and the greater part of the operation was performed under nitrous oxide and oxygen alone. At no time was there the slightest trouble. A relative apnea was quickly established and continued (more or less completely) throughout. At the end of the operation the patient was "blown out" with pure oxygen as usual. So far as Cotton and Boothby know, the only gas-oxygen apparatus which it is safe to use for intratracheal work is the one which they have recently devised, for the details of which they refer to their other papers.

The Treatment of Perforated Duodenal Ulcers.—OFFENBERG (*Zentralbl. f. Chir.*, 1911, xxxviii, 1625) says that the treatment of a perforated duodenal ulcer cannot be uniform, but must depend upon the circumstances of the individual case. Whether it is to be sutured or a gastro-enterostomy done, depends not so much upon the anatomical relations of the markedly inflamed field of operation. He reports the case of a man, aged twenty-eight years, who suddenly during the night, was taken with a severe pain in the epigastrium. He has been previously well, and when attacked felt as if a knife had passed from the origin of the pain to the right lower abdominal region. On admission to the hospital, he exhibited the picture of a perforation peritonitis. Pressure in the ileocecal region produced as much pain as pressure in the epigastrium, so that an appendicitis was thought of. The operation was performed twelve hours after the occurrence of the perforation. There was found in the anterior wall of the duodenum, opposite the papilla of Vater, a round hole, out of which poured forth a well of bile and pancreatic fluid. The latter had already produced everywhere fat necrosis. At first an effort was made to suture the ulcer, but repeated efforts failed because of the fragility of the tissues. Since time was pressing, a posterior, retrocolic gastro-enterostomy was immediately performed. After cleansing the peritoneum, a tampon was pressed strongly against the ulcer opening to prevent the escape of the intestinal fluid. The liver was then pressed down on the ulcer and fixed in this position by gauze pressed in between the surface of the liver and the costal margin. The wound was closed in the usual way, and the usual precautions taken. The gauze tampons were gradually removed during the after-treatment. The patient left his bed fourteen days after the operation. The fear of a duodenal fistula was not realized. The liver pressed down on the ulcer opening, acted like a valve in closing it, and the liver was not separated from it after the removal of the tampons.

Substitution of the Esophagus by a Plastic Operation on the Stomach.—HIRSCH (*Zentralbl. f. Chir.*, 1911, xxxviii, 1561) says that while the technique of gastrostomy is so highly developed, much remains to be desired, even in successful cases, and we ought to aim at a plastic substitution of the esophagus that will permit the patient to introduce the food by his mouth. Roux accomplished this purpose by using a resected piece of the jejunum, but this has obviously many disadvantages. Hirsch proposes to make an esophagus from a flap taken from the anterior wall of the stomach. The abdomen is opened by an incision from the sternum to the umbilicus. The stomach is drawn out as far

as possible, and from the anterior wall is made a long rectangular flap, consisting of the whole thickness of the wall, with its base above turned as much as possible toward the lesser curvature to provide the best nourishment (the vessels of the anterior wall come chiefly from the lesser curvature). This flap is turned upward, and the defect in the stomach closed by layer suture. This suture is continued upward without interruption to the flap, which is sutured around a tube to form the new esophagus. The stomach is returned into the abdomen, and the abdominal wall closed. The junction of the new esophagus with the stomach is sutured to the upper end of the abdominal wound by the peritoneal suture, which was left long for the purpose. This prevents at this point a kinking of the esophagus as it is coming out of the abdomen. It is then conducted under the skin of the thorax, and its upper end fixed as high as possible, so that at a later operation it can be made to communicate with the normal esophagus. Experiments on the cadaver showed that the flap from the normal stomach can be brought up easily to the neck. If the stomach cannot be drawn out of the abdomen, the operation cannot be done. The study of injected specimens from the cadaver showed that there were always several branches of the left superior gastric artery which entered the flap and continued to its end. In operations on dogs the flaps were preserved. Physiology teaches that in swallowing the mass of food passes to the stomach in less than a tenth of a second—*i. e.*, before the contraction of the pharyngeal and esophageal muscles occurs. This contraction follows the act of swallowing and forces down only the remains of the swallowed mass or large masses. Hirsch has not yet had an opportunity to perform the operation on the human as the indications are limited and the cases, therefore, few. He thinks that the principle can be applied to other hollow organs, as in the substitution from the bladder of a portion of the ureter or the urethra.

A New Manipulation during Narcosis.—GONTERMAN (*Zentralbl. f. Chir.*, 1911, xxxviii, 1626) says that to the indispensable implements for anesthetization belong the mouth gag and tongue forceps. What unpleasant sensations are left after the use of the tongue forceps are well known, as are the complaints of the patient concerning pain at the angle of the jaw from the use of the mouth gag. Gonterman substitutes for both the following method of accomplishing the same purposes: With the head in the low position, after opening the mouth with the gag, a broad, round, gauze pad, 3 to 4 cm. thick, held on a handle, is introduced on the side of the mouth opposite the gag. In order that the tongue already, fallen back, may not be forced further back, and at the same time that it may be lifted forward and later held there, it is desirable that the introduction of the pad with the handle holding it, should be made with a rotating movement, so performed that the tongue is lifted forward. The pad is then rolled on the surface of the tongue until it rests on the base in front of the epiglottis, when the tongue will be resting on it. By pressing it forward in the direction of the submental region not toward the opening of the mouth, which would allow it to slide off, the tongue is lifted forward. The epiglottis follows this movement, and the larynx is kept open. It is easy to hold the instrument in this way during the whole operation, but it is ren-

dered more easy by resting the shaft of the handle on the upper teeth. Since the pad gradually becomes saturated with mucus, it must be changed from time to time. After the introduction of the pad and handle the mouth gag is no longer necessary and should be removed. The laying on of the mask for anesthesia is only slightly influenced by this method. Gonterman has employed it in many cases, in some lasting several hours, and has found it very satisfactory.

THERAPEUTICS

UNDER THE CHARGE OF

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The Indications of Treatment with Lime-poor Food.—HIRSCHBERG (*Berlin. klin. Woch.*, 1911, xlviii, 2056) says that it has been proved that there is an abnormal amount of lime salts in the articular cartilages in cases of arthritis deformans. Schüller has had favorable results in the treatment of arthritis deformans by limiting the amount of lime in the diet, and Hirschberg substantiates his results by similar effects obtained by him in the treatment of this disease and other forms of arthritis. Hirschberg puts these patients on a test diet with an approximate lime content expressed as CaO of 1.86 grams. If no more than 10 per cent. of this lime is eliminated in the urine he considers that there must be retention of lime. The diet is then changed to one poor in lime, and these patients are kept on this lime-poor diet for six to eight weeks. The chief articles to be avoided in a lime-poor diet are milk, butter, yolk of eggs, potatoes, and spinach. Other vegetables are given in small amounts, and distilled water only should be allowed with the diet. Hirschberg found that a marked improvement was obtained in many severe joint affections, as measured by both subjective and objective symptoms. This improvement was especially notable in cases with marked ankylosis of the spine of the Bechterew and Strümpell-Marie variety. Likewise, notable benefit was observed in cases of arthritis deformans and in joint pains following acute attacks of multiple joint inflammation.

Creatin and Creatinin in Animal Metabolism.—THOMPSON and WALLACE (*Brit. Med. Jour.*, 1911, 2652, 1065) believe that the retention of creatin, whether given with food or formed in the body, is intimately connected with carbohydrate metabolism. They found that the excretion of creatin in the urine apparently bore a direct relation to the severity of the glycosuria in 3 cases of diabetes. The addition of creatin in doses of 1 grain to the diet of the mildest case had no appreciable effect on the output of sugar. Coincidently there was a marked diminution in the excretion of creatinin in these cases

of diabetes that showed the increase of creatin excretion. The administration of creatinin in doses of 0.15 to 0.18 gram, either given hypodermically or with the food, temporarily increased the excretion of sugar nearly 50 per cent. From this they raise the practical point that soups, meats, and meat extracts rich in creatinin should be excluded from the diabetic diet.

The Physiological Action of Amorphous Digitoxin-digalen.—SYMES (*British Med. Jour.*, 1911, 2655, 1346) relates animal experiments regarding the physiological action of digalen that seem to support the conclusions that digalen is an active preparation of digitalis producing characteristic effects on the circulatory system and on the secretion of urine. Intravenous, subcutaneous, and intramuscular injections have produced no local trouble. Symes believes that the human subject in immediate need of digitalis will react more satisfactorily to the administration of the drug intravenously.

The Treatment of Amebic Dysentery.—ANDRESEN (*Med. Rec.*, 1911, lxxx, 1024) believes that the ipecac treatment of amebic dysentery is by far the best method. This method of treatment has been in use in India for many years, and is now the accepted method of treating amebic dysentery in the Philippine Islands. He gives the details of the treatment, for he believes that close attention to details is necessary to secure the best results. The patient is best put upon a liquid diet or a light diet leaving only slight residue. An initial dose of castor oil is administered, and cold enemata are given twice a day. The cold enemata may be a saline solution; quinine solution, 1 to 500; or thymol, 1 to 2000. These enemata relieve tenesmus and wash out debris, but it is almost certain that local antiseptics have no effect upon the amebæ in the colon. The ipecac is best given in 5-grain salol- or keratin-coated pills. A pill larger than 5 grains is very difficult to swallow, and may not readily pass the pylorus. Ipecac is best given about eight o'clock in the evening, and no food should be given for four hours before the treatment is begun. It is usual to give about 20 minims of tincture of opium a short time before the ipecac is to be given. The initial dose of ipecac should be large, Simon recommending as much as 40 or 60 grains. Andresen has found that excellent results were obtained with an initial dose of 30 or 40 grains. If the pills are properly coated, the patients frequently do not vomit at all. If they do vomit, the vomitus usually consists of a small amount of clear mucus. If vomiting is more marked and distressing, it may be controlled by application of ice-bags to the throat, mustard paste to the epigastrium, or by hypodermic injections of morphine. The dose is reduced 5 grains every evening until the dose has reached 10 grains, and this dose is continued for two weeks. The smaller doses often give rise to more nausea and vomiting than do the large initial doses, and it may be necessary to decrease the dose still further until a point of tolerance is reached. This dose is then continued for about two weeks, even though there are no active symptoms of the disease. Andresen says that, under this form of treatment, the diarrhea stops within a day or two, and scrapings made from the rectum as early as forty-eight hours after the first dose fail to reveal the amebæ. The ulcers

frequently heal in less than a week. The first week or ten days of the treatment should be spent in bed. After the first two or three weeks of treatment a more liberal diet is allowed, but the return to a normal diet should be gradual. When the treatment has been thoroughly carried out, complications are rare, and return of the condition after months or years is much less common than after other methods of treatment.

The Diagnosis of Gout by Therapeutic Test with Atophan.—ZUELZER (*Berlin. klin. Woch.*, 1911, xlvii, 2101) has observed that the increased elimination of uric acid in gouty subjects after the use of atophan is associated with a marked diminution in the uric acid content of the blood. This increased elimination of uric acid and diminished uric acid content of the blood go hand in hand with a marked improvement in the clinical symptoms. Weintraud and others have found that uric acid injected intravenously into gouty patients is rapidly excreted when atophan is given at the same time, while, on the other hand, if atophan is not given, gouty individuals retain the injected uric acid for a long time. They have also found that the same increase of uric acid excretion occurred when the sodium salt of nucleic acid was given with a simultaneous dose of atophan. They believe that the chief etiological factor in gout is an inability of the kidney to excrete uric acid. They explain the action of atophan in gout by a direct and selective stimulating action of atophan upon the kidney that increases its ability to excrete the uric acid. Zuelzer does not believe that this explanation is sufficient, although it may be partially true. He believes that the increased elimination of uric acid in gouty subjects following administration of atophan is of diagnostic value in differentiating true gouty affections from non-gouty joint inflammations. He says that the urine of a true case of gout under treatment with atophan will show an abundant urate deposit sufficient to be recognized by the gross appearance of the urine. This deposit of urates will not occur in non-gouty patients. There are, of course, exceptions to this general rule, but Zuelzer believes that this rough test will differentiate the majority of cases of true gout. He adds a note regarding the good results obtained by him in the treatment of recent cases of neuralgia with atophan.

Recovery of a Typhoid Bacillus Carrier during Vaccine Treatment.—BREM and WATSON (*Arch. Int. Med.*, 1911, viii, 630) review the literature of the treatment of typhoid bacillus carriers. Eleven recoveries have occurred, and 5 of these patients recovered during vaccination with autogenous vaccines. Brem and Watson report the case of a child from whose urine typhoid organisms in pure culture were isolated one month after her discharge from hospital. The child was treated with antogenous vaccines, nine doses in all being given with an initial dose of 25,000,000, gradually increased to 1,500,000,000. Eleven successive urine cultures were positive during the period of treatment, that continued six months after the acute symptoms of the attack of typhoid fever. During the next three months five successive cultures were negative for typhoid bacilli.

The Treatment of Pernicious Anemia with Intramuscular Injections of Defibrinated Blood.—Esch (*Deutsch. med. Woch.*, 1911, xxxvii, 1943) reports a case of pernicious anemia with a red blood count of 448,000, and a hemoglobin percentage of 22, successfully treated with intramuscular injections of defibrinated blood. He injected 35 c.c. of defibrinated blood taken from a woman whose blood showed 70 per cent. of hemoglobin. Dyspnea, nausea, and vomiting ceased after the first injection, and there was a considerable improvement in the general condition of the patient. Three more injections were given in the course of two weeks, and at the end of this time the hemoglobin had risen to 53 per cent. Five injections were given in all, in amounts of from 25 to 70 c.c., and at the end of two months the hemoglobin percentage was 75, with no subjective symptoms of the disease.

Salvarsan.—Ehrlich (*Münch. med. Woch.*, 1911, lviii, 2481) gives a brief review of some of the more important articles on salvarsan therapy. He says that the consensus of opinion is that salvarsan is a relatively harmless drug. A number of fatalities ascribed to salvarsan have been shown to be due to entirely different causes. The fever and constitutional symptoms at first attributed to salvarsan are due to the use of old distilled water, and they may be avoided by using water freshly distilled to make up the salvarsan solution. Ehrlich says that salvarsan therapy has simply brought into prominence the subject of nerve recurrences, and these have been falsely cited as evidences of salvarsan poisoning. He says that a close study of reports of cases treated with mercury has shown that nerve recurrences are more common after treatment with mercury than after salvarsan therapy. Ehrlich advises the combined treatment of syphilis by giving the salvarsan in a large dose and following it up with active mercurial treatment by means of intramuscular injections. The list of diseases favorably influenced by salvarsan therapy is a large one, and Ehrlich names those in which it exerts a more or less specific action. This list mainly comprises those diseases that are caused by some form of spirillum. Among these are fowl spirillosis, recurrent fever, yaws, tertian malaria, Aleppo boil, bilharzia, pneumonic plague of horses and African farcy. Ehrlich does not believe that it is possible to improve upon salvarsan, since this remedy was the result of long experimentation, as its former name "606" implies.

The Therapeutic Use of Iodine in Nascent State.—Kaufman (*Berlin. klin. Woch.*, 1911, xlviii, 2251) has had good results in treating various local conditions by the application of a potassium iodide solution that is followed by the use of a solution of hydrogen peroxide. He says that iodine is set free from the iodide solution in its nascent state by this method. The amount of iodine set free is controlled by the strength of the solution used. Thus he uses from very dilute solutions of the iodide up to the maximum limit of a 5 per cent. solution, and the hydrogen peroxide solution in varying strengths from 0.1 to 1 per cent. A solution of sodium perborate with the addition of a small amount of citric acid may be used in place of the hydrogen peroxide solution. He claims that this method is very efficacious in various catarrhal affections of mucous membranes, particularly in subacute or chronic urethritis.

PEDIATRICS

UNDER THE CHARGE OF

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Colon Irrigation: The Short vs. the Long Tube.—HENRY T. MASCHELL (*Archiv. f. Pediatrics*, 1911, xxviii, 837) prefers the short rectal nozzle to the rubber catheter in giving colon irrigations to children. Some of the objections to the rubber catheter are that it often kinks, shutting off the flow; that it curls on itself, and the tip appears at the anus; that it causes more irritation and discomfort, since it must be introduced by a series of pushes or shoves, and that traumatism to the mucous membrane is possible if the catheter is stiff or carelessly inserted. The small nozzle, on the other hand, is easily inserted, and gives a minimum of anal irritation. It is also practically safe to be used by untrained attendants. Maschell gives an analysis of 200 consecutive irrigations on infants, comparing the short nozzle and the rubber catheter alternately. The analysis shows that for the "amount injected" the short nozzle had the advantage, and that it was retained for a longer time with the short nozzle. The fluid can be made to reach the cecum by using the short nozzle, and the irritation and discomfort is less than with the catheter.

The Physiological Significance of Calcium Deficiency in Breast-fed Infants in the First Year.—W. DIBBELT (*Berlin. klin. Woch.*, 1911, xlviii, 2062) determined the amount of calcium necessary to each 100 grams increase in body weight, and applying this to Cammerer's table for the rate of body growth, formulated the amount of calcium necessary for each month of life during the first year. He then compared this table with one showing the amount of calcium the child derives normally from the mother's milk per month and found that for the first six months of life there is a marked difference between the supply and demand of calcium. For instance, in the first month the demand is 0.3246 grams, and the supply through the mother's milk is 0.1512 grams. Aron and Schabad, making similar observations, place the percentages slightly larger than Dibbelt, but show the same difference in supply and demand for the first six months of life. It must also be considered that a calcium content of 0.05 per cent. in mother's milk, upon which these tables are based, is often not reached, and the calcium content may be very much lower. During the earlier months of life there occurs in the skeleton, and especially in the long bones, a porosis, or absorption, and the calcium contents of the bony system becomes reduced. That this is a physiological process was apparently proved by Thomas in a number of experiments on puppies and kittens. He found the same reduction in the ash-content in these animals at the corresponding age period. Comparing the results from animal and human investigation, Dibbelt concludes that in all suckling animals,

from birth to the first doubling-period of weight, the body and the skeletal system develop under the influence of a calcium deficiency. The process of absorption of bone occurring after birth which enlarges the marrow-space and makes room for the red bone-marrow, is accompanied by a certain loss of calcium. At this period a nourishment poor in calcium salts would tend to assist this process of bone absorption. Herein Dibbelt sees the physiological significance of calcium deficiency in the first six months of life, which makes possible and encourages the natural process of bone absorption taking place at this period. The pathological significance in this relation appears when the calcium deficiency of a nourishment for the first six months falls too far below the determined necessary 0.04 or 0.05 per cent. Seemann and Pfeiffer's analyses of the milk of mothers whose infants were rachitic show a calcium content varying from 0.029 per cent. to 0.019 per cent., and 0.17 per cent. instead of the required 0.04 to 0.05 per cent. Dibbelt produced disturbances of the calcium content in the bones of suckling puppies which gave clinical symptoms similar to those of beginning rickets by feeding the dam with a diet almost free from calcium. The end of the first six months of life marks a period of lowered skeletal resistance. The attendant calcium deficiency in the nourishment may predispose to a subsequent condition of rickets. The establishment of rickets in the first year of life is associated with the influence the calcium salts exert on the child's body and skeletal system.

Clinical and Bacteriological Observations on Influenza in Infants.—Erich Müller and Erich Seligmann (*Berlin. klin. Woch.*, 1911, xxxvi, 1636) report the clinical and bacteriological findings on a large number of cases of influenza in infants. Only the unusual forms of this disease are discussed. Two forms are particularly mentioned: One, in which a clinical picture of sepsis is developed; the other, in which there are suddenly developed formations of exudate in the serous cavities of the body. The septic type is characterized by very sudden intermissions of temperature and variations between 40° C. and 37° C. No organic lesions can be demonstrated, and the general condition of the child is not, as a rule, seriously affected. While many of these cases recover completely within a few days, other cases are seen which either become prostrated at the onset, or, after repeated relapses, sink after weeks into a septic condition and die, without even the autopsy showing any special organic lesion. A further danger of this type of cases is the possibility of infecting other children, since such cases are often prolonged throughout the summer with their varying periods of normal temperature. Among the types exhibiting the formation of an exudate, that affecting the pleura in the form of an empyema is relatively frequent. The empyema may develop at the onset or after several days. The prognosis is usually bad, especially with rib resection, etc. A minimum of shock, with just enough incision to relieve the pressure somewhat, and a gradual drainage have given the best results in these cases. Still more hopeless are cases in which the exudate occurs in the peritoneal cavity. Here also the localizing signs may develop immediately, simulating a primary peritonitis; or, after several days of indefinite illness, the peritoneal symptoms set in with a sudden rise in the temperature. Distention of

the abdomen is the first ominous sign, and the superficial veins on the abdomen are prominent. The course of the disease is here rapidly fatal, with septic symptoms. The bowel movements are normal or slightly dyspeptic, and vomiting, while it occurs, is not a prominent symptom. Convulsions occur in the later stages. Autopsy shows a purulent exudate with marked formation of fibrin. A local cause for the condition was not found in these cases, the appendix in particular being intact. The infection, therefore, occurs directly from the bowel or, more probably, through the blood stream. Müller and Seligmann report a number of cases showing cerebral symptoms, with bulging fontanelle and convulsions. Lumbar puncture indicated a serous meningitis, with high pressure and a sterile fluid, and the autopsy verified this, although the process had not formed an exudate, which might easily occur in subsequent epidemics. Besides the influenza, bacillus of Pfeiffer, which does not play the chief role in the influenza of infancy, many other organisms have been found as etiological factors, especially pneumococci (Esherich) and diplobacilli (Trumpp). This being the case, the disease known as "grippe" clinically combines a number of different infectious diseases, from an etiological standpoint. In this epidemic referred to by Müller and Seligmann cultures from the throat (50) showed regularly diplococci and streptococci, which, however, were not characteristic when cultured. Influenza bacilli, diplobacilli, and pneumococci were routinely absent. However, a microörganism was isolated twice from discharging empyemas. This coccus showed individual characteristics, differed culturally from the ordinary cocci, and was subsequently found routinely in the blood and organs of children dying from grippe. The identical coccus was found in 8 different cases. In the blood after death these cocci are small and occur singly, or attached by twos or threes. Chains of more than five or six were never seen. These are found also in septic conditions and in cases with exudate. The same organism is found regularly in the lung tissue, in the spleen, and occasionally in other large organs. Lumbar puncture was sterile. This microörganism seems to be a coccus belonging to the group of streptococci, but differing from them culturally to such a degree that Müller and Seligmann accept it as the causal organism of that epidemic and call it the grippe-streptococcus.

A Case of Amyotrophic Lateral Sclerosis in Childhood.—Boldt (*Med. Klinik*, 1911, vii, 1773) reports a case of amyotrophic lateral sclerosis occurring in an otherwise healthy boy aged eight years. This disease is very rare in childhood, occurring usually in middle-aged persons. The boy's father, grandfather, and an uncle suffered from paralysis agitans. Following an attack of influenza with fever, the boy showed a weakness of the left arm and leg. On examination the following symptoms were found: Patellar and Achilles reflexes greatly increased; Babinsky and Oppenheim signs positive on both sides; marked paresis of the left arm and leg, and slight paresis of the right leg. After treatment for two and one-half months the disease had advanced rapidly. The left arm was completely spastic and paralyzed, and the muscles atrophied. The muscles of the left leg showed characteristic rigidity. Paresis was marked in the right leg and beginning

paresis was present in the right arm. There was stammering speech, frequent aphonia and constant swallowing; widening of the palpebral fissure and paralysis of the abducens, the latter of rare occurrence in this disease. The symptoms increased in severity until the child's death two months later. Sensibility remained intact throughout the course of the disease. On the basis of a congenital weakness of his motor system, the child developed, through a febrile infectious disease, a typical symptom complex of lateral sclerosis. It is possible that the febrile attack was not influenzal, but the febrile reaction of the onset of lateral sclerosis. The unusually rapid course of the disease is remarkable. According to Oppenheim the usual duration is from two to four years; in this case it was only five months.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Eclampsia.—LICHTENSTEIN reports from Zweifel's clinic in Leipsic the results in the treatment of 400 cases of eclampsia (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1). He finds that in all eclamptics convulsions cease in but one-third of the cases after pregnancy has been terminated. The common belief that eclampsia occurring in the puerperal period has a low mortality rate was shown to be incorrect. The mortality of the induction of labor is not better than that following the rapid emptying of the uterus, and the mortality of both procedures does not differ especially from the general mortality of a large series of cases. The most modern statistics are not favorable to the emptying of the uterus. The difference in the mortality between eclampsia before and after labor seems to depend upon the relative loss of blood, and this is from 100 to 150 c.c. of blood more than the average loss in labor. In 40 per cent. of eclamptics operated upon, the average blood loss of eclampsia, reckoned at 500 c.c., is exceeded during operation; while in those who are delivered spontaneously there is no increase in the blood loss; 52 per cent. of eclamptic patients operated upon have a greater blood loss than that occurring in normal labor; while but 4 per cent. of eclamptics delivered spontaneously exceed the average blood loss of parturition. Those patients in whom convulsions cease after delivery lose one-half more blood than those in whom the convulsions do not cease, and four times as much blood as those in whom the convulsions first develop during the puerperal period. The significance of blood loss is seen most strikingly in its tendency to produce collapse. If the loss of blood in eclampsia is to be beneficial, it is better that blood be taken before the uterus is emptied, instead of encouraging bleeding during the rapid termination of pregnancy. That the interruption of pregnancy in eclamptic

patients is not imperative is proved by those cases in which the eclampsia ceases and the pregnancy continues to its normal termination, often with the birth of a living child. When one attempts to reason concerning the placental theory of eclampsia, by comparing the results of rapid delivery and induced labor in eclampsia with former statistics, the placental theory receives from this source no support. Cases of intercurrent eclampsia do not support the theory that eclampsia is produced by the product of conception. It is further observed that eclampsia often first develops during or after the birth of a macerated fetus, which must have been dead for some time. In the psychoses which follow eclampsia, it is found that these patients have two or three times as many convulsions as the general average—eight for each patient. In 50 cases which came to autopsy, dilatation of the ureters and pelvis of the kidney was found in 30 per cent.; while in 27 patients operated upon before death, it was found present in 33⅓ per cent.

The Vaginal Extirpation of the Pregnant Uterus in Phthisical Patients.—Heil (*Zentralbl. f. Gynäk.*, No. 44, 1911) has operated upon 7 cases. One of these died of phthisis six months after the operation; 3 survived from one year to one year and one-half, and are still in good condition; in 2 the pulmonary condition is markedly improved; while in the last case operated upon the tuberculosis seems to have made progress. In selecting patients for operation he would take those who have already given birth to children now several years old and in good condition. The tuberculous process in the lungs must be clearly defined and increasing. The lung tissue must not be hopelessly diseased, for should this be the case substantial improvement cannot be expected. He prefers vaginal total extirpation of the uterus to operations upon the tubes, because the latter are not absolutely certain in their results. In multigravidæ two or three months advanced the operation is especially successful. In later pregnancy the anesthesia and blood loss are unfavorable. In recommending this method of treatment, Heil accepts the reasoning of Martin, who more than a year ago urged the adoption of this procedure.

Rupture of the Uterine Scar after Classic Cesarean Section.—Vogt (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1) contributes an interesting paper on this subject. His observations were made in Leopold's clinic in Dresden, and he reviews to some extent the literature on the subject. He distinguishes between the time before antisepsis and the period subsequent to this when antiseptic and aseptic precautions have been observed. In the first period up to 1886, Krukenberg had collected 18 cases of rupture of the scar after Cesarean section. At this time the uterus was not sutured after operation, and Krukenberg believed that the scar ruptured in 50 per cent. of these patients who again became pregnant. Winckel observed 4 cases of rupture in subsequent pregnancy in labor. Afterward Saenger, in 1882, urged the exact closure of the uterus by suture. In 1895 he reported that in 500 cases where the uterus had been exactly closed, rupture in the scar had been observed. After this the operation was taken up by many operators, some of whom were unskilled surgeons, and in 1905 Werth had collected 12 cases of rupture. In 1908 Hartmann collected 18

cases, and since then others have in all found 22 cases. Among the French, Couvelaire in twenty years had collected 8 cases. In 183 operations von Leuwen found four ruptures. Vasseur estimated that rupture occurred in 2 per cent. of cases. Excessive amniotic liquid and twin pregnancy predispose to rupture. The attachment of the placenta beneath the uterine scar is also favorable to this accident. The site of the uterine incision seems to have no influence upon rupture, for it occurs in both the longitudinal and transverse incision. So far as suture material is concerned, rupture has been observed in cases where silk was used, silk and catgut, and catgut alone. It is observed that cases which heal without infection and by primary union are much less apt to rupture than those in which infection develops and union is secondary. There is very much more in the method of applying sutures than in the choice of suture material. An experienced and skilful operator who closes the uterus accurately and thoroughly will have a very small percentage of ruptures in the scar. It is, however, true that the possibility of rupture in subsequent pregnancy can never be entirely eliminated. This is true if gonorrheal infection has been present at the time of the original operation, or subsequently. In clinics having the largest number of operations, the smallest percentage of ruptures has been reported. Olshausen, in 120 cases, observed rupture in the scar but once; Braun, in 77, in none; Everke, in 64, in one; Chroback, in 64, had none; Schauta, in 177, had none; Küstner, in 100, had none; and Leopold, in 232 cases, had no case of rupture in the scar. As regards cases of repeated section, Olshausen, in 29 cases, had operated upon 2 patients twice, and upon 3 patients three times. In the Leipsic clinic, in 54 cases, there were 11 done a second time and 4 done three times. Braun, in 74 cases, did the operation twice on 5 patients, and three times on one patient. Küstner, in 104 cases, operated twice on 10 and three times on one. Leopold, in 229 cases, had 15.5 per cent. of repeated section. Birbaum operated four times upon a patient successfully, but after the fifth operation the patient died of pulmonary embolus. Braun and Vogt have reported cases of induced labor after Cesarean section in which the uterine scar remained sound. Spontaneous labor after Cesarean section is comparatively rare, Braun reporting but 3 cases, and Abel, from the Leipzig clinic, but 2 cases. In an ape that had been subjected to section a spontaneous labor with living young afterward occurred. In cases where the subsequent labor is terminated by the use of forceps, or by version, the scar is naturally put to the severest test. Kroback did version in 2 cases, in 1 of which symphysiotomy preceded version. Abel had 3 induced labors after section, and in 2 cases embryotomy was performed. To illustrate what such a patient can endure without injury, Vogt reports the case of a woman having a flat rachitic pelvis with a true conjugate of $6\frac{3}{4}$ to 7 cm. She was delivered three times by craniotomy, once by version, in the fifth and sixth pregnancies by Cesarean section. In the seventh pregnancy the patient had twins, one of which was born spontaneously, the other developing the transverse position. In the eighth pregnancy version and perforation of the after-coming head were performed. In the ninth pregnancy the patient declined any operation, and after fourteen hours of labor in Walcher's position the head was brought by pressure through the pelvic brim, and a child 52 cm. long and weighing

3000 grams was delivered. The cranium showed the results of pressure, but the child recovered and subsequently became vigorous. This delivery was preceded by version, and an excellent opportunity was given to test the firmness of the scar. The mother made an uninterrupted recovery. In Lihotzky's case, five years after section the patient had induced labor. Rupture did not occur in the old scar, but in the uterine muscles some distance from the scar. Krukenberg reports 3 similar cases. Füth performed section upon a patient who had an incarcerated dermoid cyst in the pelvis which prevented delivery. In the second labor, as the pelvis and the size of the child were normal, no operative interference was practised, but the uterus ruptured, not in the scar but near the place of entrance of one of the Fallopian tubes. A similar case occurred in the Dresden clinic in a patient who had been delivered by section two years previously for eclampsia. In a second pregnancy induced labor was undertaken outside the clinic, and the patient was brought to the hospital with symptoms of peritonitis. On performing section the child and placenta were found in the abdominal cavity, and the uterus ruptured through the right cornu, but not in the old scar. A Porro operation was performed from which the patient made a good recovery. The mortality of this accident is estimated by Scipiades as about 45 per cent. In the collection of 22 patients, 3 died—a mortality of 13 per cent.; in 8 the wound in the uterus was again united; in 13 some method of amputation was practised. The prognosis for the child is naturally bad; 31 per cent. are saved by prompt operation. It is important in these cases to know how great has been the first blood loss, and whether, when the patient is seen, the bleeding has ceased or is going on. The second point depends upon whether the ovum has been totally expelled or partially retained. If the placenta has been delivered, the empty uterus contracts and bleeding from the placental site ceases. The point of rupture usually bleeds but little. In some cases the primary blood loss is sufficiently great to be fatal. Occasionally patients are able to walk or to be carried for some distance after the accident. In one case the patient did not collapse until the bursted uterus contracted upon a loop of intestine which had prolapsed into its cavity. Microscopic studies of these cases show that where union is successful muscular tissue develops so perfectly that no trace of the original scar can be found. Where muscular tissue is lacking and the connective tissue replaces it, the danger of rupture is greatest. It is the opinion of experienced operators that at the present day so perfect is the technique of the operation that the danger of subsequent rupture is very slight. In 162 cases of cervical section Holzapfel had no case of rupture of the scar. Traugott found the cervical scar greatly thinned and dilated in a case subjected to a second operation. Sellhein has also seen a similar case. A study of this subject leads one to conclude that in order to prevent rupture of the scar the uterus must be accurately and thoroughly closed and heal without infection. A patient who has had a section, and with whom the possibility of conception remains, should pregnancy again occur, should be under the observation of a physician, and convenient to a clinic. In the event of rupture, operation should be done as quickly as possible, and the operator must decide whether he will endeavor to save the uterus, or remove it. A classic Cesarean section is not only a life-

saving operation for the child, but in the hands of skilled operators is especially such for the mother. Rupture of the scar, after an operation properly performed, is exceedingly rare, and with good surgical attention has a very favorable prognosis.

Hemolysis by Streptococci in the Vaginal Secretion of Pregnant and Parturient Patients.—A contribution to this complicated and controversial subject is made by LAMERS (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1). His experiments lead him to conclude, with Frommes, that the germs found in a particular patient are harmless to that patient, even though they may be in a condition favorable for the development of hemolysis. Those germs which are transferred from without to a patient are the real producers of severe infection. The mere occurrence of hemolysis does not make the difference between these germs, but is a question as to the energetic growth of the bacteria. It is the relation of the germs to the patient which is important. We have as yet no method of determining accurately whether a given germ is potent or inert to a given patient. Lamers concludes that hemolytic streptococci are found in the genital tract, and in the secretions of pregnant patients, not as a rule, but as an exception to the average. The presence of hemolytic streptococci in the lochial secretion cannot be explained as an increase of germs already present during pregnancy, nor is it probable that these germs were introduced by examinations made during labor; it is also not probable that these germs arise from the ascent of bacteria during confinement or the puerperal period. In pregnant parturient and puerperal women, one often observes colonies of greenish streptococci weakly hemolytic, which must be considered as intermediate forms between those which are not hemolytic and those which are. It seems probable that the hemolytic can develop from the non-hemolytic. Those hemolytic streptococci which develop without disturbance to the patient, and without fever, seem to come from the non-hemolytic germs. On the contrary, those which do produce fever and other symptoms arise from germs introduced from without. Hemolysis produced by streptococci does not depend so much upon the individual germ as upon the surroundings favorable for its development.

GYNECOLOGY

UNDER THE CHARGE OF

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Relation of Ovulation to Menstruation.—FRAENKEL (*Zentralbl. f. Gyn.*, 1911, xxxv, 1591) has found by observations made during abdominal operations for extragenital conditions that a fresh corpus luteum is never found in the ovaries when the operation is done during the period of menstruation, therefore ovulation and menstruation do not

necessarily occur together. In 43 cases where a fresh corpus luteum was present the time which had elapsed since the beginning of the last preceding menstrual period varied from eleven to twenty-six days, but the average of most cases was eighteen to nineteen days. Allowing four days for formation of the ripe corpus luteum, this may be considered to begin to functionate about ten days before the following menstrual period. Fraenkel considers the corpus luteum the causative factor in bringing about the premenstrual changes in the uterine mucosa and in causing menstruation, and points out that its beginning to functionate about ten days before the next succeeding menstruation corresponds well with the Hitchman and Adler doctrine of the premenstrual alterations of the endometrium. The formation of the corpus luteum occurs, therefore, in the *intermenstruum*, in the second half of the interval between two periods, so that while ovulation and menstruation do not occur together, they do stand in direct time relation to each other. Fraenkel makes an appeal to all surgeons who have the opportunity to make observations along this line to do so and record their results, as only from a large amount of material can trustworthy conclusions be obtained.

Ascending Kidney Infection.—An attempt has been made by SUGIMURA (*Virchow's Arch.*, 1911, ccvi, 20) to demonstrate the method by which acute non-specific bladder inflammations reach the kidney. For this purpose he examined 21 cases, removing at autopsy the kidneys, ureters, and bladder together, and taking in each case microscopic sections from the pelvis of the kidneys, various portions of the ureters, and the bladder wall. In 4 of these cases the organs were apparently healthy, in 12 an acute bladder inflammation was present, but the pelves of the kidneys were macroscopically free, in 5 a severe inflammation of the upper urinary tract was present, associated with a more or less chronic cystitis. In the cases of apparently normal organs no inflammation of importance was found in the ureters. In those of acute cystitis the muscularis, adventitia and submucosa of the ureters almost without exception showed, at least in the lower portion, many small foci of inflammatory infiltration which were in direct connection with those of the bladder wall. The mucosa itself was found, on the other hand, to be practically free from all signs of inflammation, such as might have been expected to be present if the infection had travelled through the lumen of the ureter. Sugimura believes, therefore, that an acute infection of the bladder ascends chiefly through the lymph vessels of the ureters, since a direct connection between the lymph vessels of the bladder wall and of the lower portion of the ureter on the one hand, and between the kidney and the ureter on the other, has been demonstrated, so that the kidney and bladder are really in communication with each other through the lymphatic vessels of the ureters. He believes further that the inflammation ascends more or less in direct proportion to the anatomical changes in the bladder wall, to the duration of the disease, and to the virulence of the causative agent. In the cases of chronic, non-specific descending inflammation with or without stagnation of urine, the important part played by the lymph vessels could also be demonstrated, although here the mucosa appeared to be somewhat more involved than in the cases of ascending infection.

Trypsin in the Uterus.—Continuing the work of Halban and Frankl, which appeared somewhat over a year ago, with regard to the presence of a proteolytic ferment in the endometrium of the menstruating uterus, FRANKL and ASCHNER (*Gyn. Rundschau*, 1911, v, 647) have attempted, by somewhat different methods to those previously employed, to determine the relative quantities of such ferments in the endometrium at the different stages of the menstrual cycle. This was done in the following manner. By means of a sharp curette the endometrium was scraped out of freshly extirpated uteri, mixed with quartz sand, and thinned with ten times the quantity of distilled water. This was rubbed until fine (about five minutes), and was allowed to stand for twenty-four hours in the ice box; it was then filtered, and to 2 c.c. of the filtrate were added 2 c.c. of a 50 per cent. weakly alkaline solution of peptone ("Seidenpepton"). The mixture was set away in calibrated centrifuge tubes in an incubator at 37° C. for twenty-four hours, whereupon there occurred a separation of yellowish-white crystals, which could be identified by various tests as tyrosin. By means of control experiments Frankl and Aschner have found that, within certain limits, a certain quantity of trypsin throws down from a given quantity of peptone a definite amount of tyrosin within a given time, so that a fairly satisfactory quantitative determination of the amount of trypsin present is possible by this method. In interpreting the findings, however, the chief weight must be laid on the *relative* quantities rather than on actual amounts. Forty cases, in each of which the exact clinical history was known, were examined by this method. It was found that in the interval the trypsin content of the uterus is very variable, the formation of the ferment beginning in one case earlier, in another later; it always increases toward the end of the interval, however, and in the pre-menstrual stage is always very considerable. In the postmenstrual stage trypsin is almost lacking under physiological conditions; under pathological conditions, however, such as glandular hyperplasia, it can be present in quite considerable quantities. Inflammatory processes accompanied by suppuration often cause a marked increase in the ferment content of the endometrium; chronic non-purulent processes do not have much effect on it. Frankl and Aschner believe that the phenomenon of menstruation is due to the pouring out in the pre-menstrual stage of this ferment, which is then *activated* by the physiological hyperemia present, as has been demonstrated by the experiments of Rosenbach. The ferment thus activated causes a swelling of the stroma-cells, a digestion of the walls of the superficial capillaries of the endometrium, and is also responsible for the non-coagulability of the menstrual blood.

Function of Ovary in Menstruation.—HALBAN (*Zentralbl. f. Gyn.*, 1911, xxxv, 1585) considers that rut in animals and menstruation in women are very closely analogous. It can be shown that rut occurs in frogs and other animals even after castration, but it does not reach so full a degree of development as in normal animals. The same is true of menstruation—in a certain number of cases cyclic molimina and even bleeding occur for some time after the removal of both ovaries. Halban believes, therefore, that neither the sexual gland itself nor any secretion from it is the fundamental causative factor in

the production of menstruation or of rut, but that these are due to some totally unknown agency which profoundly affects the whole body; the effect of this agency can only reach its full development, however, when the sexual gland is present. This therefore exercises a "protective," but not a "formative" role on the phenomena of menstruation.

Function of the Ovary.—ADLER (*Arch. f. Gyn.*, 1911, xcv, 350) has carried out a series of most elaborate experiments in the attempt to throw additional light upon this question. He has found that in most cases of amenorrhea, in women past the menopause, and in patients upon whom double oöphorectomy has been performed, the coagulation-time of the blood is distinctly longer than in normal individuals. He has also found that in the same subject the coagulation-time is increased after double oöphorectomy as compared with what it was before the operation, and believes that it is dependent upon a condition of hypofunction of the ovaries. Since it has been shown that the coagulability of the blood is dependent, among other things, upon the presence of lime, and since it is well known that there is a close relationship between the genital glands and lime metabolism, as is shown by the improvement that occurs in cases of osteomalacia after castration, it is natural to think that the lengthening of the coagulation time caused by reduction in the ovarian activity may be due to changes in the calcium metabolism in the body. Adler has found by a series of careful analytical tests that the lime content of the blood is reduced after castration, and also after *x*-ray treatment of the ovaries, and believes therefore that an intimate relationship exists between ovarian function, the amount of lime in the blood, and the coagulability of the blood. Adler has not been able to produce any apparent effect on the blood pressure by injecting extract of corpus luteum or of ovarian tissue, but did get a rise after the use of pressed ovarian juice. In a young girl whose menstruation had always been absolutely regular he was able to cause the periods to occur 4 days ahead of time, to be much more profuse than normal, and to last one day longer, by giving ovarinin for three weeks preceding the period. He has been able to produce with great regularity in animals the anatomical conditions of the uterus characteristic of rut—hyperemia, gland activity, etc.—by subcutaneous injections of various ovarian preparations, and by similar treatment of human patients has been able in many instances to cause a reduction or disappearance of the subjective symptoms of the menopause. In some cases of amenorrhea ovarinin treatment has been followed by the appearance of menstruation, in these cases microscopic examination of the endometrium showing typical menstrual changes, so that the bleeding cannot be considered merely the result of hyperemia. In conclusion he says that his investigations have shown the general type of individual to be dependent, not upon one, but upon a harmonious coördination of all the organs of internal secretion. He thinks that perhaps much which appears to be due to alterations in ovarian function is really the expression of disturbances in other organs; the ovary must be considered as the centre for the genital sphere, as a centre, however, which not only sends out independent impulses, but which also transmits impulses that it receives from the intimate and complicated system of ductless glands.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF
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Reflex Affections of the Tonsil.—FAULKNER, in a paper on "Reflex Affections of the Tonsil" (*New York Med. Jour.*, August 5, 1911), deprecates the too great prevalence of tonsillectomy, and suggests that the tonsils are often sacrificed unnecessarily.

Non-communication of Frontal Sinus and Nose.—FULLERTON reports (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) a case in which, while performing a Killian operation on the right frontal sinus, he entered a smaller left sinus containing pus and granulation tissue, but apparently without any detectable communication with the nasal fossa.

Killian's Operation in the Sinuses.—In discussing the subject of fatalities after this operation, SYME (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) expressed the opinion that the danger in Killian's operation was probably too thorough curettage of the ethmoidal regions, and therefore he considered it better to attack the ethmoid intranasally and cautiously, and to adopt Killian's procedure for the frontal sinus alone.

Meningeal Complications Resulting from Diseases of the Accessory Nasal Sinuses.—STUCKY reports (*Kentucky Med. Jour.*, June 1, 1911) 16 cases of meningeal and cerebral complications involving the silent area of the brain (anterior frontal cerebral lobes) as result of ethmodial, sphenoidal, and frontal sinus disease. Sixteen were reported, including 6 recoveries and 10 deaths, and the result of 8 autopsies are given. Among the complications it is noted that the infection originates primarily in the ethmoid cells—or their offshoot, the middle turbinated bone—the frontal and sphenoidal sinuses becoming involved secondarily, either through extension by continuity of tissue, or by blocking of their natural openings for drainage and ventilation long enough for their retained secretions to become purulent.

Removal of a Bullet Embedded in the Cribriform Plate of the Ethmoid.—DOS SANTOS reports (*Revue Hebd. de Lar., d'Otol., et de Rhinol.*, June 17, 1911) a case of attempted suicide in whom, by radioscopy, a bullet was found to have become embedded in the cribriform plate of the ethmoid, whence it was removed by external access.

Cerebral Abscesses Complicating Suppuration of the Nasal Sinuses.—ONODI (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) alludes to the statistics he has collected of 106 cases, 82 of which were secondary to frontal sinusitis, 11 to ethmoidal disease, 4 to antrum suppuration, and 1 was secondary to sphenoidal disease. Twenty-five cases of cured extradural abscess following frontal sinus suppuration were on record,

and among these there was one case in which exploratory puncture of the brain had been performed, with a negative result. In 7 of these cases the posterior wall of the frontal sinus had been perforated, and in 11 cases it was found to be diseased. In 20 of the cases of brain abscess the posterior sinus wall had been perforated, and in 57 of the cases it was diseased. In the majority of the cases the brain abscess was situated in the frontal lobe; three times it was found in the temporal lobe, once in the pedunculus cerebri, and once in the cerebellum. Of these 106 cases of brain abscess, 12 recovered as a result of operation and 29 died in spite of operation. Exposure of the cranial cavity through the ethmoidal cells in life had not yet been carried out.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Organic Matter in the Expired Breath.—WEICHARDT, of Erlangen (*Arch. f. Hyg.*, Band lxxiv, Heft 5, p. 185), calls attention to the fact that the numerous researches of Flügge and his school have shown that the very smallest bodies, such as the tubercle bacilli, can be thrown off in the expired breath during speech, coughing, or forced expiration. He believes it is self-evident that other movable particles in the respiratory tract, such as protein substances and other split products, may also be brought up and be discharged during expiration. It is obvious that fermentative processes go on in the excretory products of the respiratory tract, especially in older persons. The bronchial mucus of corpses is especially rich in toxic substances. This may be shown by injection into laboratory animals, such injections causing a sudden fall of temperature, slowing of respiration, and finally death. Fluids condensed from the expired air and then concentrated, when injected into mice, produce like results according to Weichardt. The Japanese investigator, INABA (*Zeitsch. f. Hyg. u. Infectionskrankheiten*, Band lxviii, S. 1) believes these results to be due to the anisotonic nature of the fluids injected rather than to toxins or protein poisons. Weichardt collected substances from the breath of a fatigued man, aged over sixty years. In this experiment he collected substances from the residual air, so far as possible, by passing the expired breath for two or three hours into 10 c.c. of distilled water to which was added 0.3 c.c. NHCl. The whole was quickly concentrated in vacuo to about 2 c.c., then neutralized with NaOH and divided into two parts; 1 c.c. of this solution, which is isotonic, was injected into a mouse, resulting in a sudden fall in temperature and slowing of respirations, characteristic signs of kenotoxin poisoning. The other

cubic centimeter was evaporated into dryness, and the residue taken up in 1 c.c. of distilled water and injected into a mouse without toxic effect. This is given in answer to Inaba's criticism that the results are due to anisotonicity. Weichardt also claims to have detected the presence of split proteins by experiments in vitro. The vapors from the expired breath of a fatigued old man, aged sixty-three years, were filtered through cotton and passed through 10 c.c. distilled water and then concentrated in vacuo to 3 c.c. Likewise 10 c.c. of distilled water was concentrated to 3 c.c. The two different solutions were then carried to dryness in a tared dish. The dish containing the distilled water left no visible or weighable residue. The solution containing the products of the expired breath left a residue weighing 9 mg. This residue turned brown when heated on the platinum foil and gave off odoriferous fumes. Weichardt also notes that a characteristic odor is produced when the solution of respiratory products acidified with hydrochloric acid is neutralized with sodium hydroxide. Weichardt presents further evidence of the presence of organic matter in the expired breath by means of its inhibitory power on the action of oxidizing ferments in blood. The oxidation of guaiac by blood is inhibited by the substances found in the expired breath just as diphtheric toxin, tetanus toxin, and kenotoxin prevent the same reaction. The experiment designed to demonstrate this fact consisted in constructing a series of tubes containing 1 c.c. of the fluid containing the products from the expired air. To each tube was added a convenient amount of very dilute solution of fresh blood and 0.1 c.c. guaiac indicator. Weichardt claims that the presence of this organic compound may also be found in the air of a closed sleeping room in which there are several persons. He exposed 0.25 gram of finely powdered calcium chloride in a platinum dish covered with filter paper to keep out gross particles. The next morning the calcium chloride was dissolved and the protein-split products believed to be kenotoxic in character may be demonstrated in the solution by means of the inhibition of the guaiac or epiphanin reaction. The epiphanin reaction depends upon variation in diffusion rates in the presence of antigen and antibody combinations. Barium hydrate and sulphuric acid are used with phenolphthalein as the indicator. The method is described in the *Deutsch. med. Woch.*, 1911, No. 4. Weichardt concludes that substances which are able to inhibit such an important function as the oxidase reaction of red blood coloring matter should not be longer overlooked. ROSENAU and AMOSS (*Journal of Medical Research*, September, 1911, vol. xxv, No. 1, pp. 35 to 84) have, through the reaction of anaphylaxis, recently come to the conclusion that the expired breath contains organic matter.

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